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14. ABSTRACT

The U.S. Air Force Medical Service presented the sixth annual Air Force Medical Research Symposium coordinated by the Air Force Medical Support Agency's Research and Development Division (AFMSA/SGRS). The symposium was held 2-4 August 2011 at the Gaylord National Hotel & Convention Center, National Harbor, MD. The symposium featured two half-days of plenary sessions, one and a half days of scientific presentations, and a poster session. It was organized into five tracks to include: Operational Medicine (In-Garrison Care), Enroute Care and Expeditionary Medicine, Force Health Protection, Traumatic Brain Injury (TBI) and Psychological Health, and Healthcare Informatics. These proceedings are organized into six volumes to include one that provides a general overview and all presentation and poster abstracts; the other five each address a specific track. Volume 6 contains abstracts and presentation slides for the Traumatic Brain Injury (TBI) & Psychological Health Track.

15. SUBJECT TERMS

US Air Force, Medical Service, Medical Research,Traumatic Brain Injury, Psychological Health

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a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			Nereyda Sevilla
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Proceedings of the 2011 AFMS Medical Research Symposium

Volume 6. Traumatic Brain Injury and Psychological Health Track Abstracts and Presentations

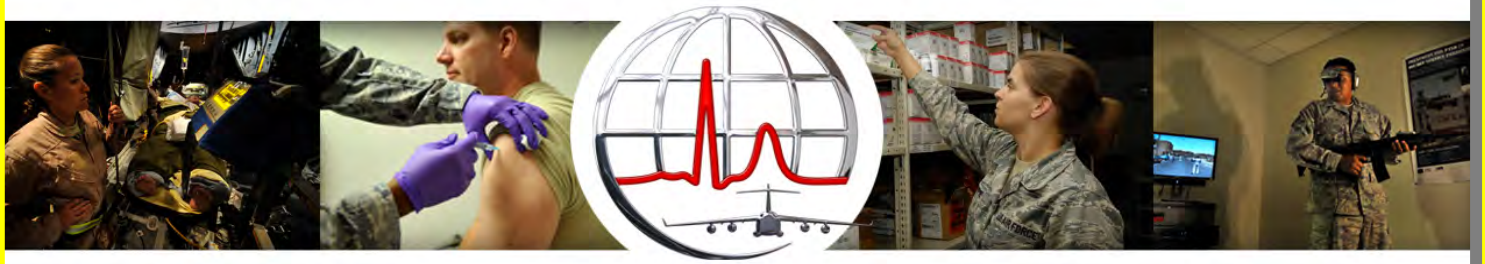
Volume 6 of 6

AIR FORCE MEDICAL SERVICE

2011 AFMS Medical Research Symposium

2-4 August 2011

GAYLORD NATIONAL
201 Waterfront Street
National Harbor, MD 20745
(1-877-677-9352)



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Proceedings of the 2011 AFMS Medical Research Symposium
Volume 6. Traumatic Brain Injury and Psychological Health Track Abstracts and Presentations

Edited by: Anderson A. Tesfazion

Held
2-4 August 2011
at the
Gaylord National Resort Hotel and Convention Center
201 Waterfront Street
National Harbor, MD 20745

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Proceedings of the 2010 AFMS Medical Research Symposium

Introduction

The U.S. Air Force Medical Service presented the sixth annual Air Force Medical Research Symposium coordinated by the Air Force Medical Support Agency's Research and Development Division (AFMSA/SGRS). The symposium was held on 2-4 August 2011 in the Washington DC area at the Gaylord National Resort Hotel and Convention Center in National Harbor, MD. The symposium featured two half-days of plenary sessions, one and a half days of scientific presentations, and a poster session.

The symposium was organized into several tracks to include Enroute Care, Force Health Protection, Healthcare Informatics, Operational Medicine (In-Garrison Care), and Psychological Health/Traumatic Brain Injury, as follows:

- The Enroute Care Track addressed science and technology targeted at the continuum of care during transport from point of injury to definitive care including, but not limited to: Casevac, Medivac; Aeromedical Evacuation; Critical Care Air Transport; and Patient Staging. Further areas addressed included: patient stabilization; patient preparation for movement; impact of in-transit environment on patient and AE crew physiology; human factors concerns for AE crew or patient population; AE/medical personnel training; infectious disease/control; burn management; pain management; resuscitation; lifesaving interventions; and nutrition research in the enroute care environment.
- The Force Health Protection Track focused on prevention of injury and illness and the early recognition or detection of emerging threats for in-garrison or deployed operations. Topics of interest include research in bio-surveillance, infectious disease, emerging threats (pandemic response), protective countermeasures, disaster response/consequence management, toxicology/health risks (e.g., particulates nanomaterials, radiation, etc.), monitoring disease trends, other areas of preventive medicine, public and environmental health relevant to the military workforce.
- The Healthcare Informatics Track focused on the use of innovative information management & technology solutions that enhance healthcare delivery at any point of the full spectrum of patient care to include medical simulation and training.
- The Operational Medicine (In-Garrison Care) Track focused on care delivered in the outpatient or inpatient in-garrison setting and on enhancing the performance of airman in challenging operational and expeditionary environments.
- The Psychological Health/Traumatic Brain Injury Track addressed topics pertaining to screening, diagnosis, and treatment of TBI and/or Psychological Health in the military community. Specific focus areas within Psychological Health included depression, substance use disorders, family functioning, and suicide prevention. Topics of special interest included field-deployable diagnostic tests for mild TBI (concussion), blast modeling, large epidemiologic studies of Psychological Health and TBI, and strategies for translating research into practice.

These proceedings are organized into five volumes, as follows:

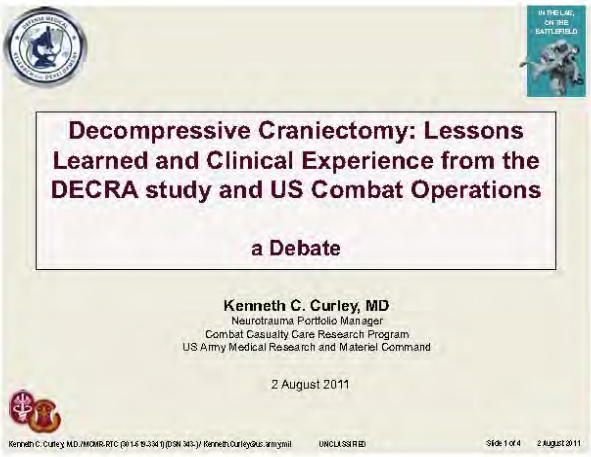
- Volume 1. This volume is a general overview of the entire 2011 Air Force Medical Research Symposium and includes abstracts of all the oral presentations and posters. First presented is the symposium's opening plenary session, followed by the abstracts from the four technical tracks, and then the closing plenary session. The abstracts associated with the poster session are in the last section of these proceedings. The agenda for the overall symposium is in Appendix A, attendees are listed in Appendix B, and continuing education information is in Appendix C of this volume. Appendices D-J are copies of presentation slides from the plenary sessions.
- Volume 2. This volume contains abstracts and presentation slides for the Enroute Care Track.
- Volume 3. This volume contains abstracts and presentation slides for the Force Health Protection Track.
- Volume 4. This volume contains abstracts and presentation slides for the Healthcare Informatics Track.
- Volume 5. This volume contains abstracts and presentation slides for the Operational Medicine (In-Garrison Care) Track.
- Volume 6. This volume contains abstracts and presentation slides for the Psychological Health/Traumatic Brain Injury Track.

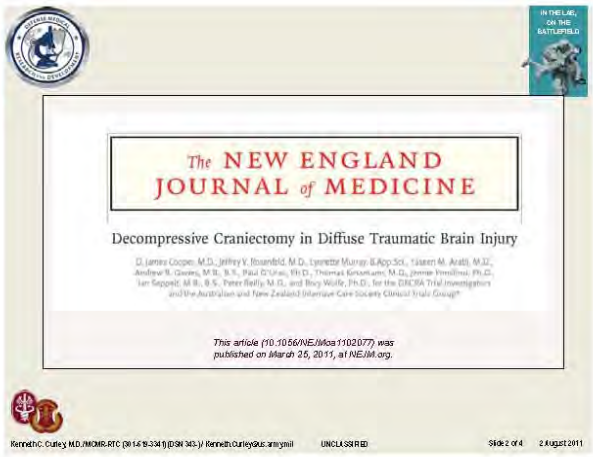
(Pro) Decompressive Craniectomy: Lessons Learned and Clinical Experience from the DECRA Study and US Combat Operations

US Army Medical Research and Materiel Command

Dr. Kenneth Curley

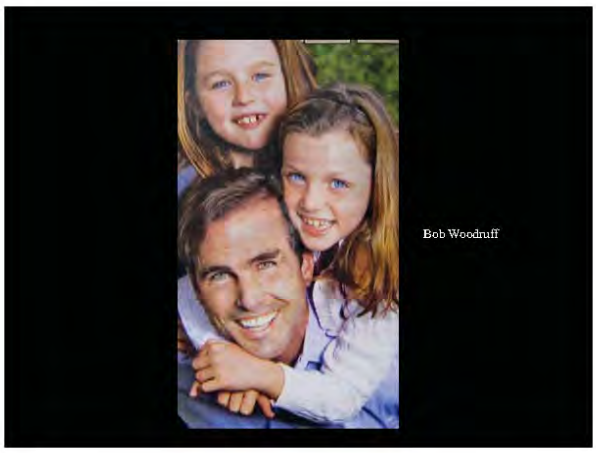
The recent publication of the DECRA (Decompressive Craniectomy or DC) trial has resulted in a great deal of discussion and disagreement especially within the military neurosurgical community.1-4 The trial was an international effort sponsored and coordinated by the Australian and New Zealand Intensive Care Society Clinical Trials Group. It was a prospective, randomized trial involving 155 adults (out of 3478 screened) with severe TBI and medically refractory Intracranial Hypertension (ICH) that found that decompressive craniectomy did not improve functional outcomes at 6 months after injury when compared to a group randomly assigned to receive non-surgical second tier ICP therapy. **Col McCafferty** and **Dr. Marion** will opine that many aspects of the trial make this one of the most important recent clinical trials of a novel therapy for severe TBI, and a Class I study that should be considered as the foundation for an evidence-based guideline. The most important is that this was a very well planned, carefully crafted and closely monitored multi-center prospective randomized clinical trial (PRCT), and PRCTs are the gold-standard for evidence based guidelines. By design, the study addressed all 22 elements of the CONSORT guidelines.5 Detailed protocols for critical care of all patients were clearly defined, agreed upon by all study investigators, and implemented at all enrolling centers. In particular, all patients were required to have intracranial pressure (ICP) monitors, 20 mm Hg was defined as the treatment threshold, and first and second tier ICP therapies were clearly defined. A pilot randomized trial was completed and published in 2008 as the basis for fine tuning protocols and data analysis plans, as well as providing objective data for determining the number of subjects needed to reach a two-sided type I error of 0.05 for the Phase III trial.6 Other than the imbalance in pupil reactivity, there were no significant clinical or demographic differences between the two groups. Dr. Marion and Col McCafferty will also address some of the concerns raised by their colleagues to include the issue of timing and inclusion of “lifesaving” procedure patients who had uncontrolled ICP at 72 hours as well as results of other PRCTs and reports that point to the issue of DC being more “gray” than “black and white”.

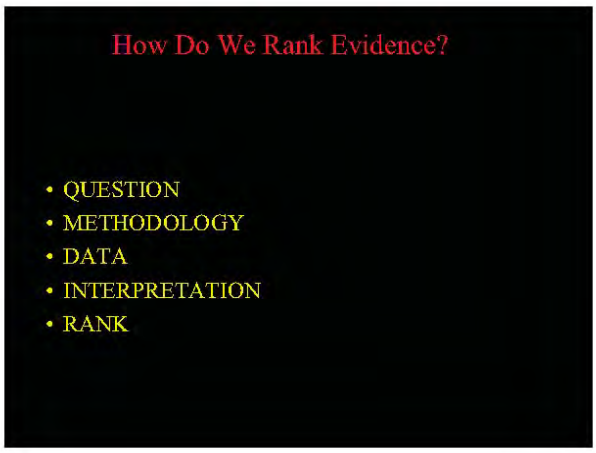

Decompressive Craniectomy: Lessons Learned and Clinical Experience from the DECRA study and US Combat Operations
a Debate
Kenneth C. Curley, MD
Neurotrauma Portfolio Manager
Combat Casualty Care Research Program
US Army Medical Research and Materiel Command
2 August 2011
Slide 1 of 4 2 August 2011

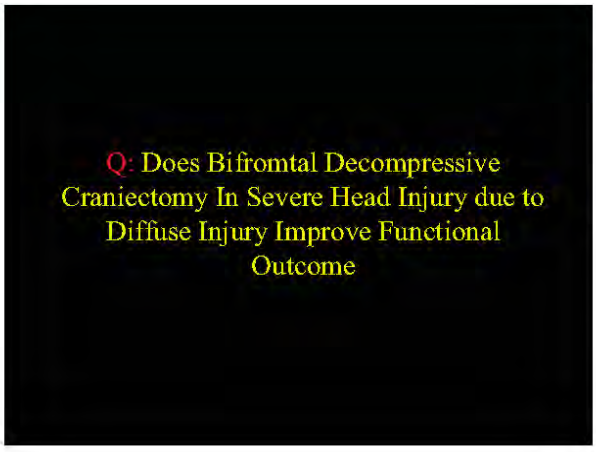

The NEW ENGLAND JOURNAL of MEDICINE
Decompressive Craniectomy in Diffuse Traumatic Brain Injury
This article (10.1056/NEJMoa1102077) was published on March 25, 2011, at NEJM.org.
Slide 2 of 4 2 August 2011

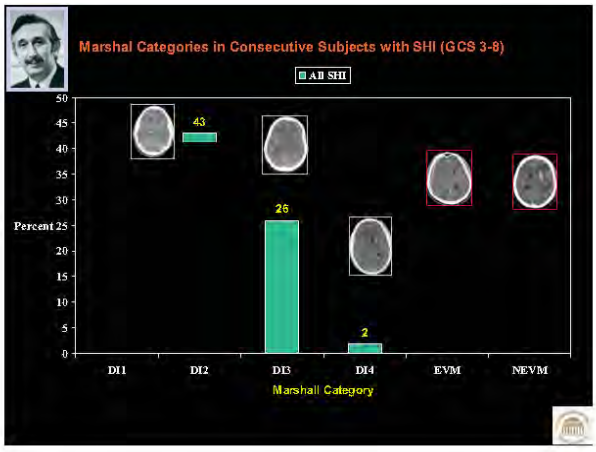

CONCLUSIONS
In adults with severe diffuse traumatic brain injury and refractory intracranial hypertension, early bifrontotemporoparietal decompressive craniectomy decreased intracranial pressure and the length of stay in the ICU but was associated with more unfavorable outcomes. (Funded by the National Health and Medical Research Council of Australia and others; DECRA Australian Clinical Trials Registry number, ACTRN012605000009617)
This article (10.1056/NEJMoa1102077) was published on March 25, 2011, at NEJM.org.
Slide 3 of 4 2 August 2011

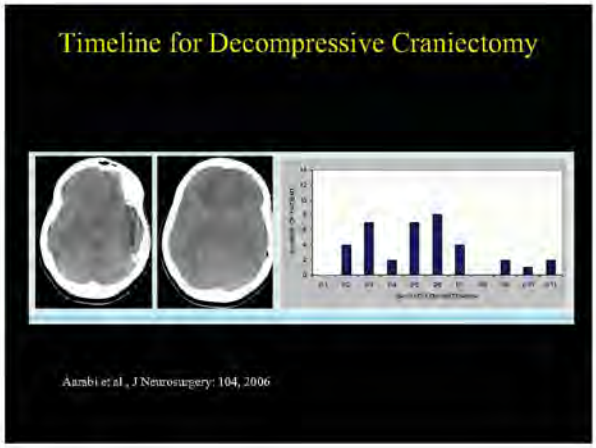

Format of Debate
• Pro-arguments
– Dr. Donald Marion,
• Defense and Veteran's Brain Injury Center
– Col Randall McCafferty,
• Chief, Neurosurgery, San Antonio Military Medical Centers
– Dr. Bizhan Aarabi
• Director of Neurotrauma, University of Maryland R Adams Cowley Shock Trauma Center
• Con-arguments
– COL Rocco Armonda
• Neurosurgery, Walter Reed National Medical Center
Slide 4 of 4 2 August 2011


Bob Woodruff

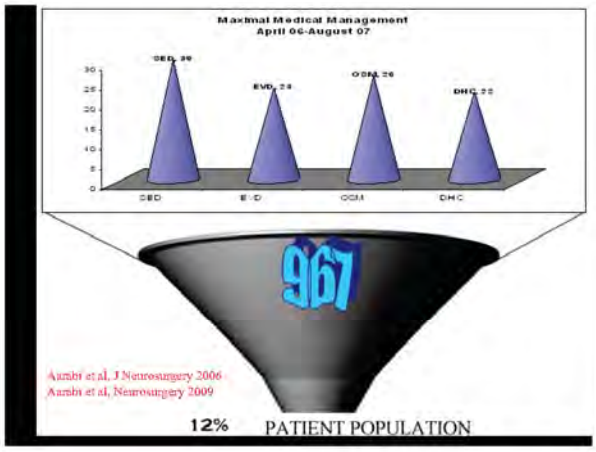

How Do We Rank Evidence?
• QUESTION
• METHODOLOGY
• DATA
• INTERPRETATION
• RANK

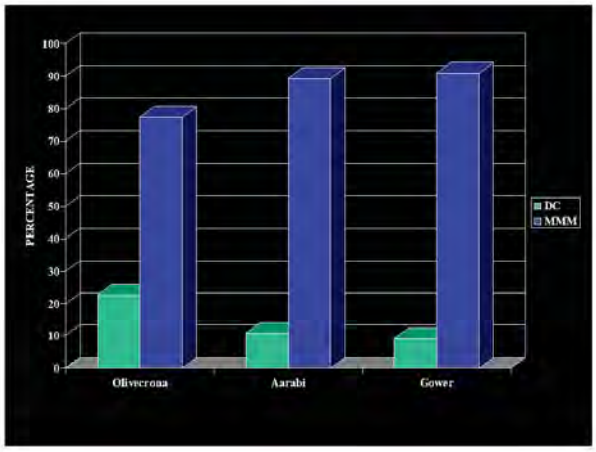

Q: Does Bifromtal Decompressive Craniectomy In Severe Head Injury due to Diffuse Injury Improve Functional Outcome

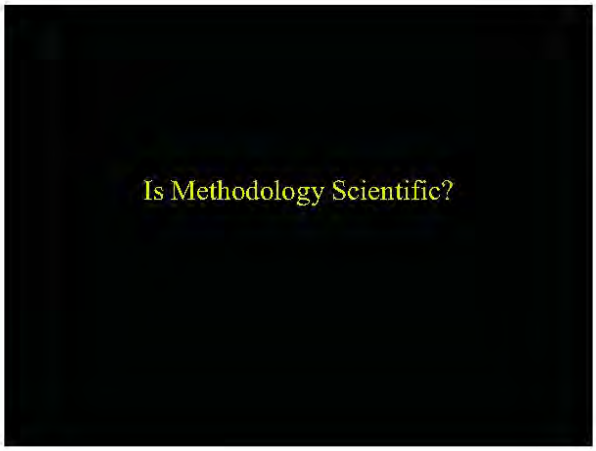

Marshal Categories in Consecutive Subjects with SHI (GCS 3-8)
All SHI
Percent
43
26
2
DI1
DI2
DI3
DI4
EVM
NEVM
Marshall Category


Timeline for Decompressive Craniectomy
Aarabi et al., J Neurosurgery: 104, 2006

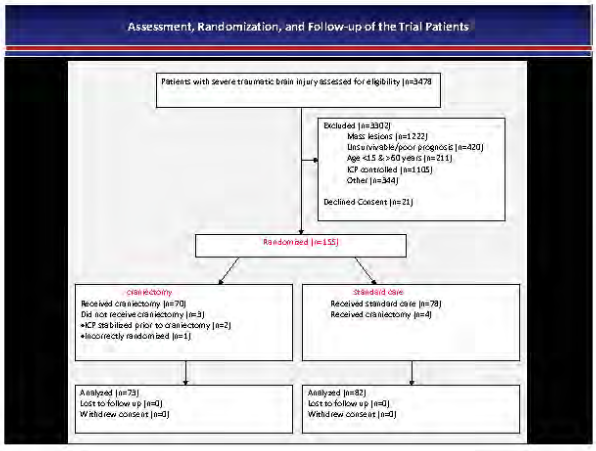

ELIGIBLE PATIENTS
MMM
DC

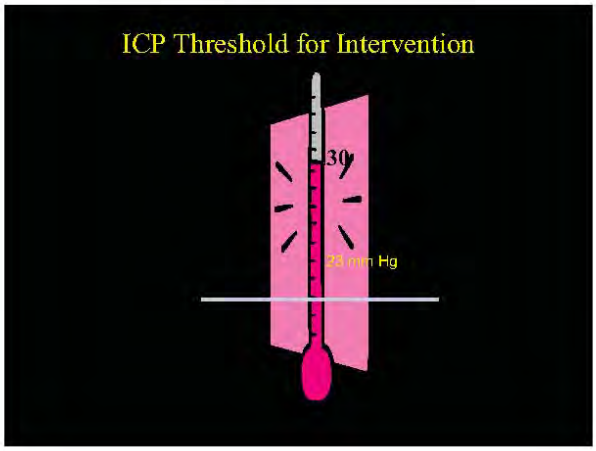

Maximal Medical Management
April 06-August 07
DED
EVD
OCM
DHC
967
Aarabi et al, J Neurosurgery 2006
Aarabi et al, Neurosurgery 2009
12%
PATIENT POPULATION

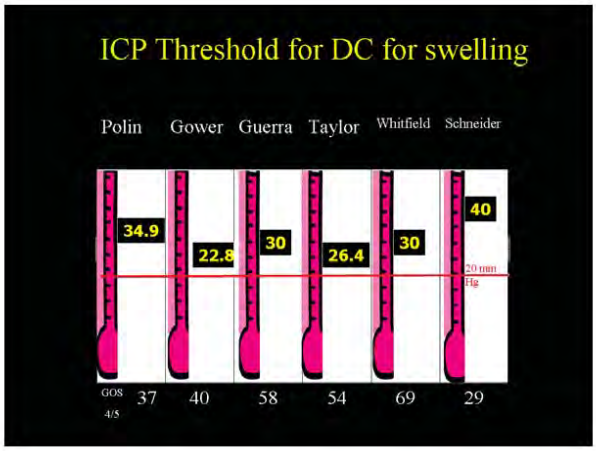

PERCENTAGE
DC
MMM
Olivecrona
Aarabi
Gower


Is Methodology Scientific?

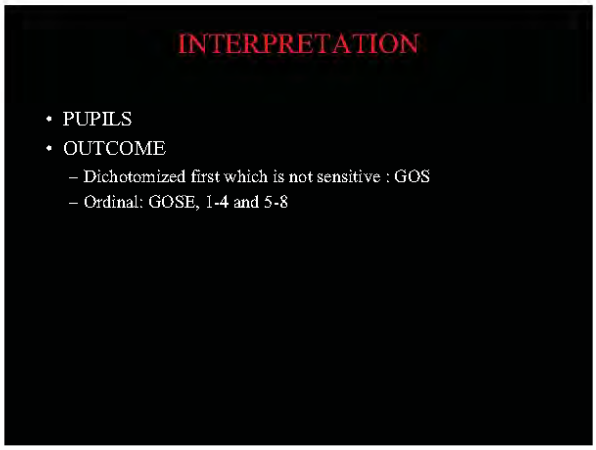

PRCT ATTEMPTS
• Coplin W
• TBI Clinical Trials Network
National Institute of Health

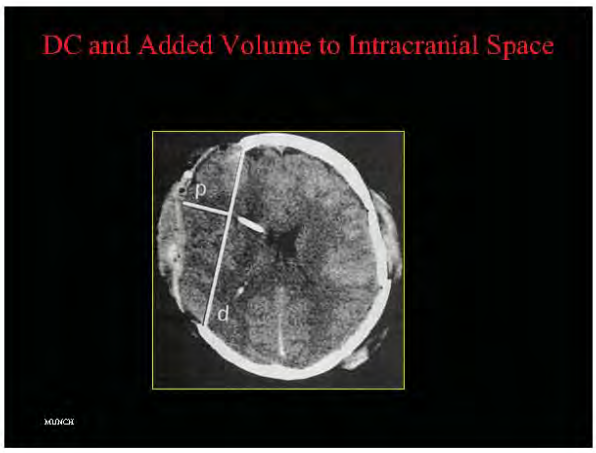

Assessment, Randomization, and Follow-up of the Trial Patients
Patients with severe traumatic brain injury assessed for eligibility (n=3478)
Excluded (n=3302)
Mass lesions (n=1222)
Unsurvivable/poor prognosis (n=420)
Age <15 & >60 years (n=211)
ICP controlled (n=1105)
Other (n=344)
Declined Consent (n=21)
Randomized (n=155)
Received craniectomy (n=70)
Did not receive craniectomy (n=3)
•ICP stabilized prior to craniectomy (n=2)
•Incorrectly randomized (n=1)
Received standard care (n=78)
Received craniectomy (n=4)
Analyzed (n=73)
Lost to follow up (n=0)
Withdrew consent (n=0)
Analyzed (n=82)
Lost to follow up (n=0)
Withdrew consent (n=0)

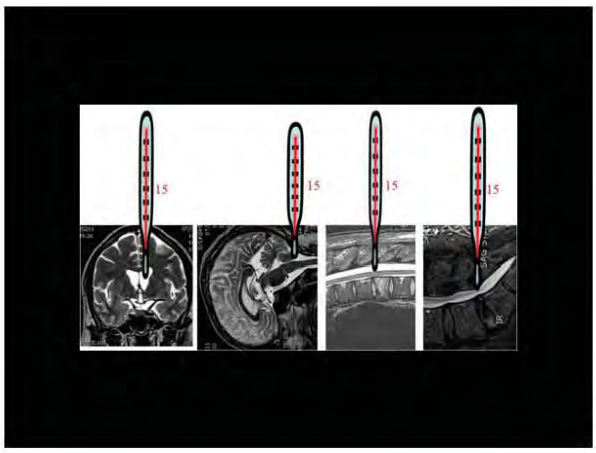

ICP Threshold for Intervention
30
28 mm Hg

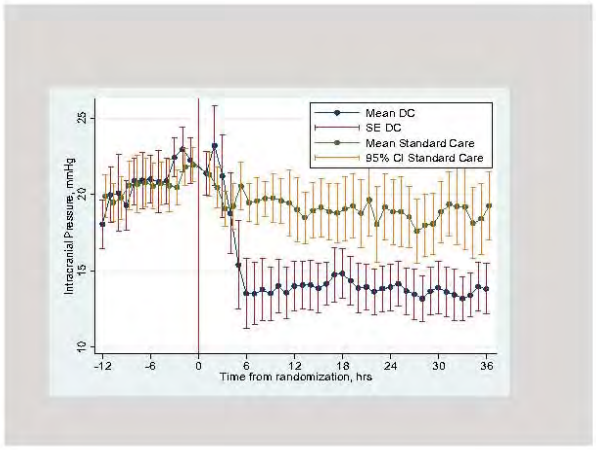

ICP Threshold for DC for swelling
Polin
Gower
Guerra
Taylor
Whitfield
Schneider
34.9
22.8
30
26.4
30
40
20 mm Hg
GOS 4/5
37
40
58
54
69
29

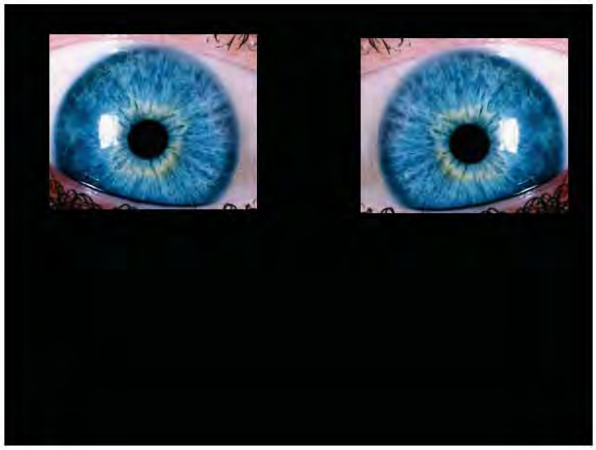

Are Data Sound & Controlled?


INTERPRETATION
• PUPILS
• OUTCOME
– Dichotomized first which is not sensitive : GOS
– Ordinal: GOSE, 1-4 and 5-8

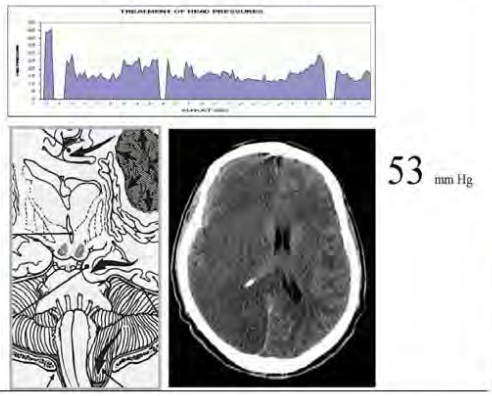

DC and Added Volume to Intracranial Space
p
d
MUNICH


15
15
15
15


Mean DC
SE DC
Mean Standard Care
95% CI Standard Care
Intracranial Pressure, mmHg
10
15
20
25
-12
-6
0
6
12
18
24
30
36
Time from randomization, hrs



DANGEROUS ICPs



35 mm Hg

53 mm Hg

Albanese et al Crit C M: 2003

PREDICTORS OF GOOD OUTCOME
Aarabi et al J Neurosurgery 2006

	Diffuse Injury		
Variable	N (% with good outcome)	Crude Odds Ratio	95% CI
Timing of DC			
Early	13 (38.5)	1.0	Referent
Late	26 (57.7)	2.2	0.6-8.5
Shift before DC			
>5 mm shift	12 (50.0)	0.9	0.2-3.6
No significant shift	27 (51.8)	1.0	Referent
Admission GCS			
3-5	12 (16.7)	1.0	Referent
6-8	18 (66.7)	10.0	1.6-60.9
9-15	9 (66.7)	10.0	1.2-78.1
Admission motor GCS			
1-4	22 (36.4)	4.2	0.1-1.16.3
5-6	17 (70.6)	1.0	Referent
Age			
<20 years	13 (61.5)	1.9	0.5-7.2
20-49 years	26 (46.1)	1.0	Referent
≥50 years	0	--	--
Abnormal pupillary response[1]	29 (58.6)	1.0	Referent
No	9 (33.3)	0.3	0.1-1.7
Yes			

RANK?

Classification of Evidence on Therapeutic Effectiveness

- Class I Evidence from one or more well-designed, PRCT studies.
- Class II Evidence from one or more well-designed comparative clinical studies.
- Class III Evidence from case series, comparative studies with historical controls.

AUTHOR	YEAR	Level of Evidence	Grade of Recommendation	COHORT	GOS 1 %	GOS2/3 %	GOS4/5 %
Gower et al	1988	IV	Weak	10	40	20	40
Gaab et al	1990	IV	Weak	37	14	8	78
Polin et al	1997	IV	Weak	35	23	40	37
Guerra et al	1999	IV	Weak	57	10	23	58
Whitfield et al	2001	III	Strong	26	23	8	69
Taylor et al	2001	II	Strong	13	23	23	54
Schneider et al	2003	IV	Weak	65	23	48	29
Timofeeve et al	2006	III	Strong	49	18.4	20.4	61.2
Aarabi et al	2006	III	Strong	50	28	32	40
TOTAL	-	-	-	342	23	25	52

Decompressive Craniectomy for Traumatic Brain Injury

Donald W. Marion, MD MSc
Defense and Veterans Brain Injury Center and the Henry M. Jackson Foundation

Disclaimer

The views expressed in this presentation are those of the author and do not reflect the official policy of the Department of Defense, Department of Veterans Affairs or the U. S. Government.

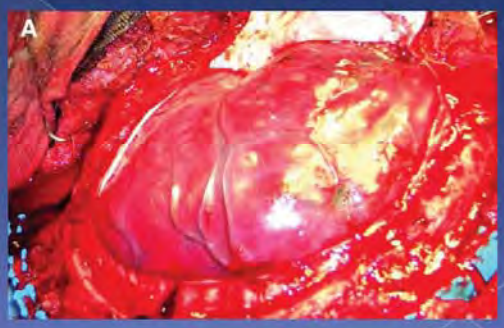
Craniectomy is necessary for non-expectant penetrating injuries

Source: ufradsite.blogspot.com

Recent studies of OIF/OEF Service Members focus on Penetrating Injuries

- Outcomes of 33 patients from the wars in Iraq and Afghanistan undergoing bilateral or bicompartmental craniectomy. Robert D. Ecker, Lisa P. Mulligan, Michael Dirks, Randy S. Bell, Meryl A. Severson, Robin S. Howard and Rocco A. Armonda. J Neurosurg, 115:124-129, 2011
  - All 33 with penetrating injuries
- Early decompressive craniectomy for severe penetrating and closed head injury during wartime. Bell RS, Mossop CM, Dirks MS, Stephens FL, Mulligan L, Ecker R, Neal CJ, Kumar A, Tigno T, Armonda RA. Neurosurg Focus. 28(5):E1, 2010.
  - 154/188 with penetrating injuries

Diffuse injury and swelling with Blast



Source: Ling, et al., JOURNAL OF NEUROTRAUMA 26:815-825 (June 2009)

DEcompressive CRAniectomy (DECRA) Trial:
First randomized trial for decompressive craniectomy

- 155 adults with:
  - Severe diffuse *non-penetrating* TBI
  - Intracranial hypertension refractory to first tier therapy
- Randomization
  - Bifrontotemporoparietal craniectomy or
  - Aggressive second tier medical management – mild hypothermia, barbiturates

Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, Kossmann T, Ponsford J, Seppelt I, Reilly P, Wolfe R; DECRA Trial Investigators; Australian and New Zealand Intensive Care Society Clinical Trials Group. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med. 2011 Apr 21;364(16):1493-502.

DECRA - Outcome

- **6 month mortality rate the same**
  - 19% (decompressive craniectomy) vs 18% (medical managment)
- **Unfavorable outcomes similar, or slightly higher for decompressive craniectomy group**
  - Adjusted OR: 1.90; 95% CI. 0.95 to 3.79
    (adjusted for higher incidence of brainstem injury in DC group)

Standards for reporting randomized controlled trials in neurosurgery
(J Neurosurg, 114:280-285, 2011)

- "...the quality of reporting of these trials remains suboptimal, especially in the neurosurgical journals."
- "Improved awareness of the CONSORT guidelines by journal editors, reviewers, and authors of these papers could improve the methodology and reporting of randomized controlled trials in neurosurgery."

Consolidated Standards of Reporting Trials (CONSORT)

- The CONsolidated Standards of Reporting Trials (CONSORT) Guidelines were developed to help authors improve reporting of two-parallel design randomized controlled trials by using a checklist and flow diagram.
- The most up-to-date revision of the CONSORT Statement is CONSORT 2010.

Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. Ann Int Med 2010;152.

DECRA Observed all but two CONSORT 2010 Guidelines

CONSORT 2010 Guidelines

Title and abstract			DECRA
	1a	Identification as a randomised trial in the title	N
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Y
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	Y
	2b	Specific objectives or hypotheses	Y

Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. Ann Int Med 2010;152.

CONSORT 2010 Guidelines

Methods			DECRA
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Y
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Y
Participants	4a	Eligibility criteria for participants	Y
	4b	Settings and locations where the data were collected	Y
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Y
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Y
	6b	Any changes to trial outcomes after the trial commenced, with reasons	Y
Sample size	7a	How sample size was determined	Y
	7b	When applicable, explanation of any interim analyses and stopping guidelines	Y
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Y
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Y
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Y
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	N
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Y
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	Y
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Y

CONSORT 2010 Guidelines

Results			DECRA
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	Y
	13b	For each group, losses and exclusions after randomisation, together with reasons	Y
Recruitment	14a	Dates defining the periods of recruitment and follow-up	Y
	14b	Why the trial ended or was stopped	Y
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Y
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Y
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Y
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Y
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Y
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Y

CONSORT 2010 Guidelines

Discussion			DECRA
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	Y
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Y
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	Y
Other information			
Registration	23	Registration number and name of trial registry (Clinical Trials.gov identifier: NCT00155987)	Y
Protocol	24	Where the full trial protocol can be accessed, if available	Y
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Y

Oxford Centre for Evidence Based Medicine, (CEBM) Evidence Grades:

(Standard endorsed by the US Agency for Healthcare Research and Quality (AHRQ), HHS)

- Evidence Grade: A
- Definition of Grade: Level 1 study
- Definition of Level 1 Study: Randomized controlled trial

Source: http://www.ahrq.gov/chipra/lessons.htm

What do the other studies show?

- There are no other randomized controlled trials that compare bilateral decompressive craniectomy with aggressive medical management!
- In 29 retrospective, or prospective case controlled/cohort studies with historical controls, poor outcomes for patients undergoing decompressive craniectomy range from 31% to 93%.

Sahuquillo J, Arikan F. Decompressive craniectomy for the treatment of refractory high intracranial pressure in traumatic brain injury. Cochrane Database Syst Rev. 2006(1):CD003983.

Criticisms of the DECRA Trial

- Crossover for medical management group
- 6 month follow-up too short
- Overly aggressive treatment of intracranial pressure (ICP) of 20-25 mm Hg
- Wrong operation

Impact of Cross-Over Design

- Intent-to-treat outcome analysis rules
- Bias is toward worse outcome in medical group

Assessment of Outcomes at 6 months- Usual Practice for Contemporary TBI Clinical Trials

- 786 patients with severe TBI in the MCV TBI Database: significant slowing in the rate of recovery after 6 months as compared to the rate of improvement from the time of injury to 6 months.
  - "the 6-month outcome could be a reasonable end point for a clinical trial".
- Trying to obtain 1, 2 and 3 year outcomes is not only cost prohibitive, but associated with significant loss to follow-up.

Choi SC, Barnes TY, Bullock R, Germanson TA, Marmarou A, Young HF. Temporal profile of outcomes in severe head injury. J Neurosurg. 1994; 81:169-173.

Overly aggressive treatment of ICP?

The number is not the whole story: How hard are you working to maintain this ICP?

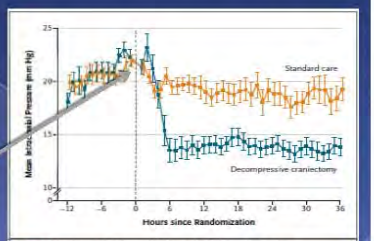
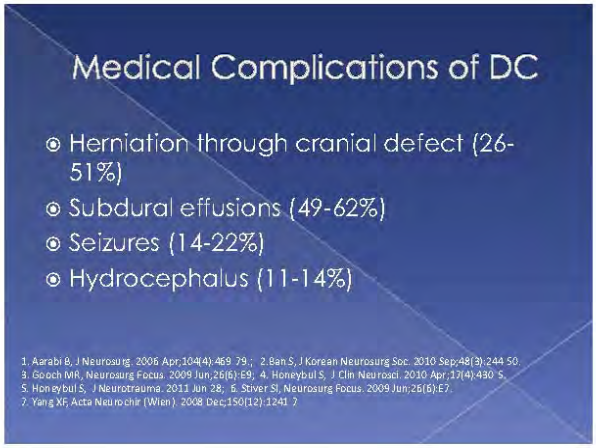
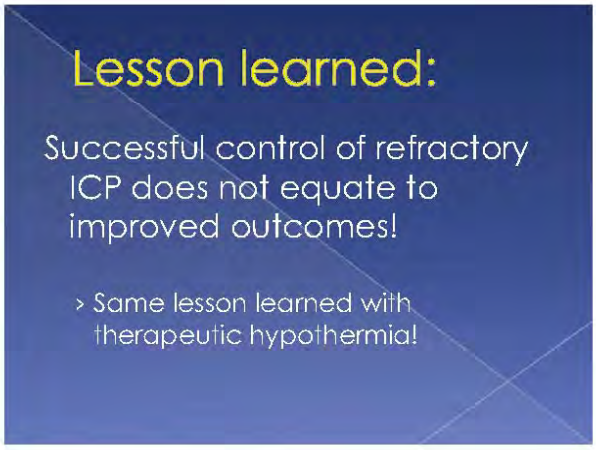


Figure 1. Intracranial Pressure before and after Randomization.
Shown are the mean measurements of intracranial pressure in the two study groups during the 12 hours before and the 36 hours after randomization. The I bars indicate standard errors.


Best Operation for Refractory ICH:
Temporal lobectomy
Extended temporal craniectomy
Unilateral frontotemporoparietal craniectomy ipsilateral to swollen hemisphere
Bilateral frontotemporoparietal craniectomy, with or without central bridge(± cut SSS, falx)
?


Medical Complications of DC
Herniation through cranial defect (26-51%)
Subdural effusions (49-62%)
Seizures (14-22%)
Hydrocephalus (11-14%)
1. Aarabi B, J Neurosurg. 2006 Apr;104(4):469-79.; 2. Ban S, J Korean Neurosurg Soc. 2010 Sep;48(3):244-50.
3. Gooch MR, Neurosurg Focus. 2009 Jun;26(6):E9; 4. Honeybul S, J Clin Neurosci. 2010 Apr;17(4):430-5.
5. Honeybul S, J Neurotrauma. 2011 Jun 28; 6. Stiver SI, Neurosurg Focus. 2009 Jun;26(6):E7.
7. Yang XF, Acta Neurochir (Wien). 2008 Dec;150(12):1241-7


Lesson learned:
Successful control of refractory ICP does not equate to improved outcomes!
› Same lesson learned with therapeutic hypothermia!


Evidence Based Standard
Decompressive craniectomy should not be considered an effective therapy for improving neurologic outcome in adults with severe nonpenetrating TBI.

Headquarters U.S. Air Force

Integrity - Service - Excellence

U.S. AIR FORCE

Decompressive Craniectomy

•Col Randall McCafferty
•AF/SG Consultant for Neurosurgery
•Chief of Neurosurgery, SAMMC

Disclaimer

- The views expressed in this presentation are those of the author and do not reflect the official policy of the United States Air Force or the U. S. Government.

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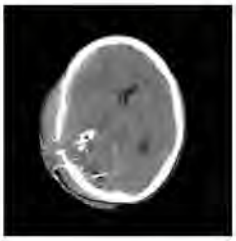
Decompressive Craniectomy

- Complications
- Military Literature
- Animal Studies



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Complications of Craniectomy

- Overall (55%)
- Herniation through cranial defect (26-51%)
- Subdural effusions (49-62%)
- Seizures (14-29%)
- Hydrocephalus (11-40%)
- ICU/Hospital stay 13/27 days

1. Aarabi B, J Neurosurg. 2006 Apr;104(4):469-75.; 2. Ban S, J Korean Neurosurg Soc. 2010 Sep;48(3):244-50.
3. Chibbaro, World Neurosurgery 75(3/4): 558-62, 2011. 4. Gooch MR, Neurosurg Focus. 2009 Jun;26(6):E9;
5. Honeybul S, J Clin Neurosci. 2010 Apr;17(4):430-5. 6. Honeybul S, J Neurotrauma. 2011 Jun 28;
6. Kan P, J Neurosurg. 105(5Suppl):337-42, 2006. 7. Paul G, J Trauma. 67(5): 531-6, 2009.
8. Silver SI, Neurosurg Focus. 2009 Jun;26(6):E7. 9. Yang XF, Acta Neurochir (Wien). 2008 Dec;150(12):1241-7.

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Complications of Cranioplasty

- Overall 34%
- Infection/Wound Dehiscence 11.6 - 14.5%
- Re-operation 26%
- Extra-Axial Hematoma 3.2%
- Status Epilepticus 1.6%
- Long term (>30d) implant problems 7 - 8%
- Death 2.2%

Gooch MR etal. Neurosurg Focus 26 (6):E9, 2009. Honeybul, et al, J Neurotrauma 28:929-35, 2011.

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Military Studies

- Bell RS, Vo AH, Neal CJ, Tigno J, Roberts R, Mossop C, Dune JR and Armonda RA. Military Traumatic Brain and Spinal Column Injury: A 5 year Study of the Impact Blast and Other Military Grade Weaponry on the Central Nervous System. J Trauma 66(4 suppl):S104-S1111, 2009.
- Ragel BT, Klimo P, Martin JE,Teff RJ, Bakken HE and Armonda RA. Wartime decompressive craniectomy: technique and lessons learned. Neurosurg Focus 28(5):E2. 2010.
- Bell RS, Mossop CM, Dirks MS, Stephens FL, Mulligan L, Ecker R, Neal CJ, Kumar A, Tigno T, and Armonda RA. Early decompressive craniectomy for severe penetrating and closed head injury during wartime. Neurosurg Focus 28(5):E1, 2010.
- Ecker RD, Mulligan LP, Dirks M, Bell RS, Severson MA, Howard RS and Armonda RA. Outcomes of 33 patients from the wars in Iraq and Afghanistan undergoing bilateral or bicompartmental craniectomy. J Neurosurg 115:124-129, 2011.
- Stephens FL, Mossop CM, Bell RS, Tigno T, Rosner MK, Kumar A, Moores LE, and Armonda RA. Cranioplasty complications following wartime decompressive craniectomy. Neurosurg Focus 28(5):E3, 2010.

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Level/Class of Evidence

Retrospective Descriptive Case Series

- Oxford Center of Evidence Base Medicine: Level IV
- US Preventive Services Task Force; National Health Centre (UK); Cochrane Collaboration: Level/Class III

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Specific Limitations of Military Reports

- Unreliable data
- High Drop Out (108/188) out of 408
  - #1 cause could not vet basic demographic info
- Not Peer-Reviewed Literature
- Difficult to obtain meaningful follow-up
- Mean GCS 7.7+/- 4.2
- "culture of care developed that all patients… potentially salvageable…undergo decompression"…'to avoid making long transport flights unsafe'

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Outcome 33 Patients with Penetrating Injury

Characteristic	GOS Score at 1–5 Yrs No. of Patients (%)	
	Poor Outcome (Score 1–3)	Good Outcome (Score 4 or 5)
focus of initial injury		
bifrontal	2 (17)	13 (72)
all other locations	10 (83)	5 (28)
timing		
delayed	0 (0)	3 (18)
early	16 (100)	14 (82)

Mean age 24
GOS at 6 mos: 17/33 GOS 4/5 (52%)

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Medical Complications from Decompressive Craniectomy in Military Patients

- Seizure 33%
- CNS infection 38%
- Shunt 14/22 (64%)
- ICU days 19.4 +/- 31.5

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Complications of Cranioplasty from Theater Patients

- Infection 12%
- Seizure 7.4%
- Extra-axial Hematoma 7.4%
- Re-operation 11%
- Death 1%

Stephens et al. Neurosurg Focus 28 (5):E3, 2010

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Neuro-Physiological Studies

- Normal Cat brain: Hemicraniectomy decreases CBF, CMRO2 and CMR
- Patients with Cranioplasty have decreased phosphocreatine activity before and significant improvement after cranioplasty
- Improved CBF after cranioplasty

Schaller, Brain Research 982:31-77, 2003. Yoshida et al. J Neurol Neurosurg Psych 61:166-71, 1996
Sakamoto et al. Clin Neurol Neurosurg 108:583-5, 2006

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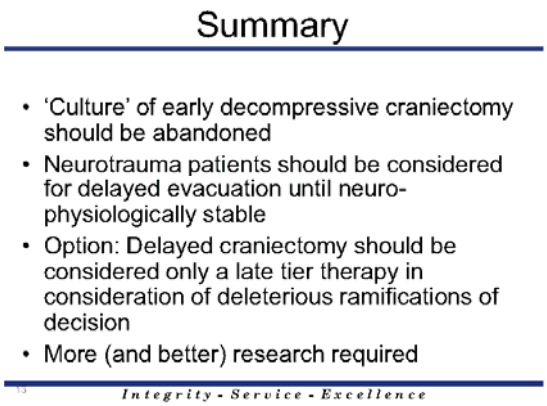
Summary
• 'Culture' of early decompressive craniectomy should be abandoned
• Neurotrauma patients should be considered for delayed evacuation until neuro-physiologically stable
• Option: Delayed craniectomy should be considered only a late tier therapy in consideration of deleterious ramifications of decision
• More (and better) research required
13
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(Con) Decompressive Craniectomy: Lessons Learned and Clinical Experience from the DECRA Study and US Combat Operations

Dr. Kenneth Curley

The recent publication of the DECRA (Decompressive Craniectomy or DC) trial has resulted in a great deal of discussion and disagreement especially within the military neurosurgical community.1 The trial was an international effort sponsored and coordinated by the Australian and New Zealand Intensive Care Society Clinical Trials Group. It was a prospective, randomized trial involving 155 adults (out of 3478 screened) with severe TBI and medically refractory Intracranial Hypertension (ICH) that found that decompressive craniectomy did not improve functional outcomes at 6 months after injury when compared to a group randomly assigned to receive non-surgical second tier ICP therapy. Issues related to severity of injury, timing of intervention, duration of followup and differences between the operated and non-operated groups with respect to injury severity were just a few of the weaknesses identified in the study.2 Of concern, many in the neurosurgical and neurological critical care communities have taken this study as evidence to support discontinuing the practice of early DC. This, despite the fact that literature published by military and civilian neurosurgeons in the U.S. have shown significant benefit in the young, healthy population. In one study 60% of the casualties were functioning independently at long-term followup.3-6 In this session**, COL Rocco Armonda** and **Dr. Bizhan Aarabi** will discuss their experiences regarding DC in contrast to what was revealed by the DECRA trial. They will argue that there is a place for DC in the military and civilian neurocasualty and that the broad interpretation of the conclusions of the DECRA trial are inappropriate.

DECRA CON: Why DECRA Doesn't Apply to Wartime Severe Neurotrauma*

Col. Rocco A. Armonda, MD
National Capital Neurosurgery Consortium
Walter Reed National Military MEDCEN

*(and probably Civilian Trauma as well)

Disclamier

- The views expressed in this presentation are those of the author (me) and do not necessarily reflect the official policy or position of the Department of the Army, Department of the Navy, Department of Defense, nor the US Government.
- I have no relevant financial disclosures

Progression of Therapy

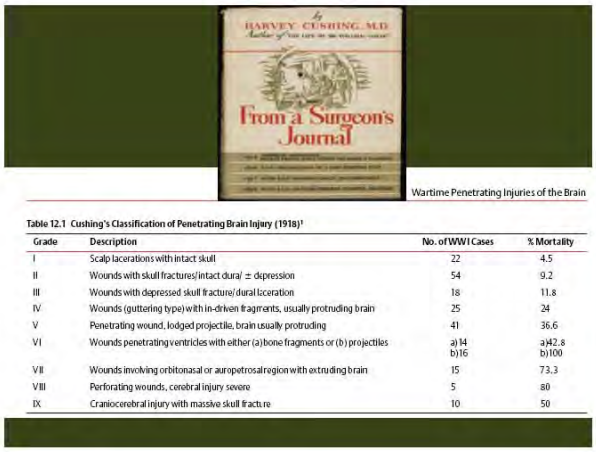
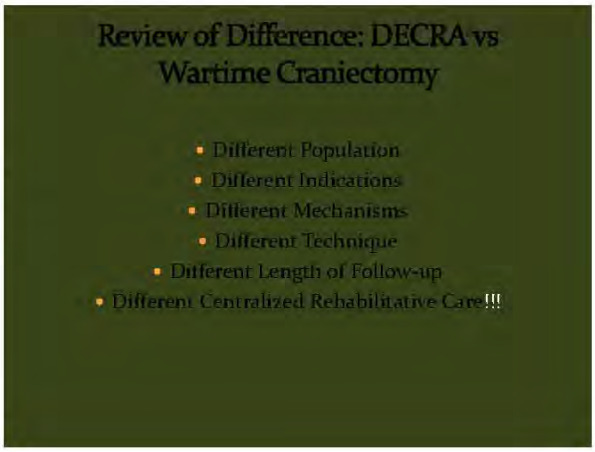
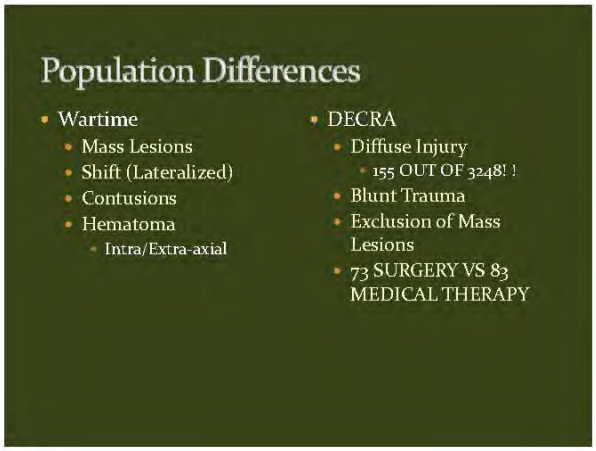
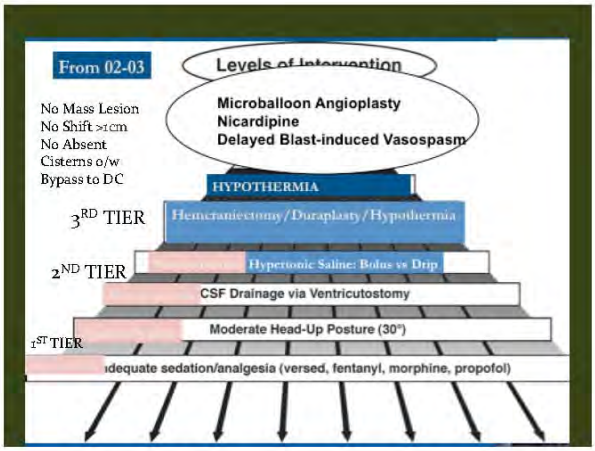


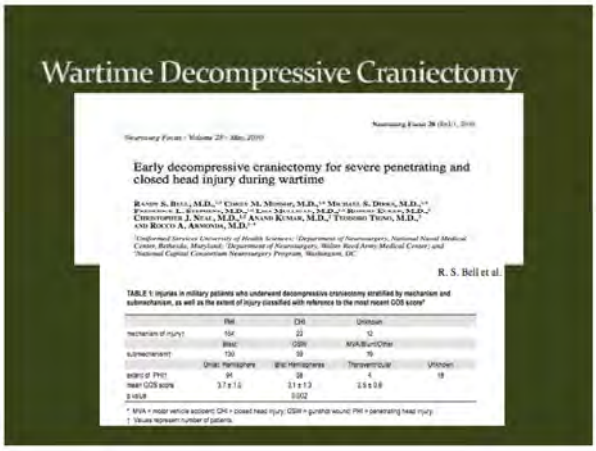
Table 12.1 Cushing's Classification of Penetrating Brain Injury (1918)[1]

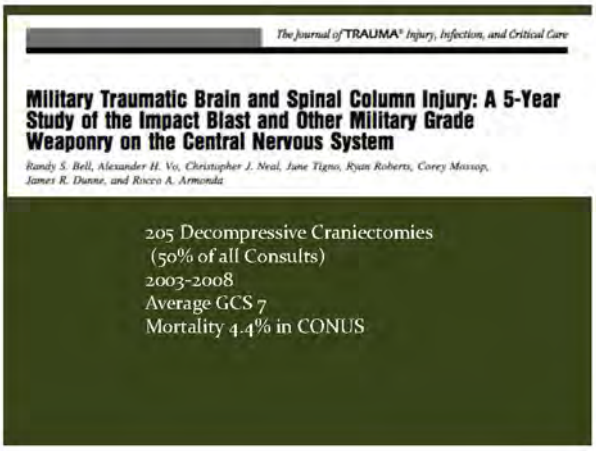
Grade	Description	No. of WWI Cases	% Mortality
I	Scalp lacerations with intact skull	22	4.5
II	Wounds with skull fractures/intact dura/ ± depression	54	9.2
III	Wounds with depressed skull fracture/dural laceration	18	11.8
IV	Wounds (guttering type) with in-driven fragments, usually protruding brain	25	24
V	Penetrating wound, lodged projectile, brain usually protruding	41	36.6
VI	Wounds penetrating ventricles with either (a) bone fragments or (b) projectiles	a) 14 b) 16	a) 42.8 b) 100
VII	Wounds involving orbitonasal or auropetrosal region with extruding brain	15	73.3
VIII	Perforating wounds, cerebral injury severe	5	80
IX	Craniocerebral injury with massive skull fracture	10	50

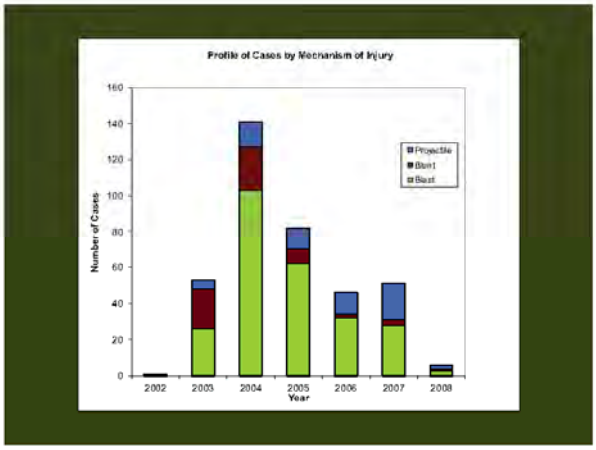


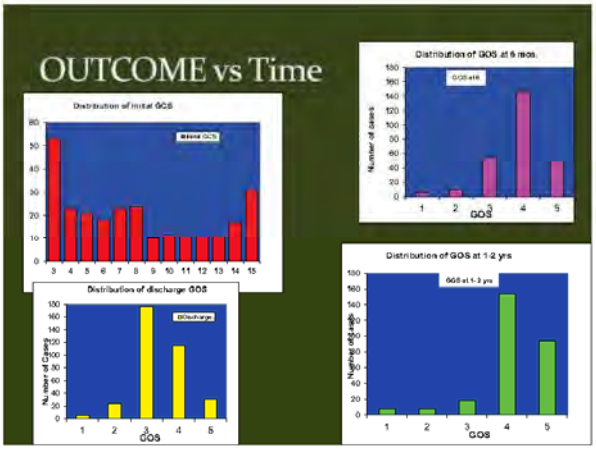





Wartime Decompressive Craniectomy
Early decompressive craniectomy for severe penetrating and closed head injury during wartime
R. S. Bell et al.


The Journal of TRAUMA® Injury, Infection, and Critical Care
Military Traumatic Brain and Spinal Column Injury: A 5-Year Study of the Impact Blast and Other Military Grade Weaponry on the Central Nervous System
205 Decompressive Craniectomies
(50% of all Consults)
2003-2008
Average GCS 7
Mortality 4.4% in CONUS


Profile of Cases by Mechanism of Injury
Number of Cases
Year
Projectile
Blunt
Blast


OUTCOME vs Time
Distribution of GOS at 6 mos.
Distribution of GOS at 1-2 yrs
GOS

Worse Group OUTCOMES

- 42 Patients with GCS 3-5
  - 17 Improved to GOS 4 or 5
  - 10 Expired
  - 15 GOS 2 and 3.

MILITARY MULTIPLE COMPARTMENT DECOMPRESSIONS

DOI: 10.3171/2011.2.JNS101490

Outcomes of 33 patients from the wars in Iraq and Afghanistan undergoing bilateral or bicompartmental craniectomy

Clinical article

Robert D. Ecker, M.D., LCDR, USN,[1] Lisa P. Mulligan, M.D., CDR, USN,[2] Michael Dirks, M.D., CPT, USA,[2] Randy S. Bell, M.D., LCDR, USN,[2] Meryl A. Severson, M.D., CDR, USN,[2] Robin S. Howard, M.A.,[2] and Rocco A. Armonda, M.D., COL, USA[2]

[1]Maine Medical Partners Neurosurgery & Spine, Scarborough, Maine; [2]Department of Neurosurgery, National Naval Medical Center, Bethesda, Maryland; and Departments of [2]Neurosurgery and [2]Clinical Investigation, Walter Reed Army Medical Center, Washington, DC

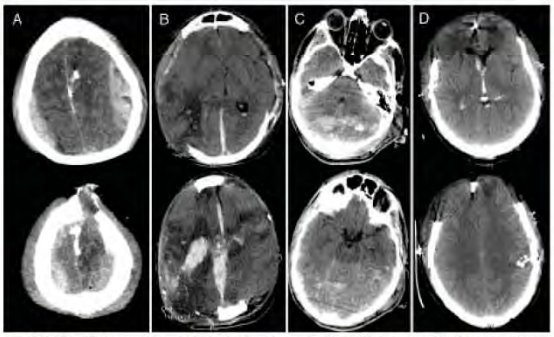


FIG. 1. Computed tomography scans showing injury focus above the ventricles (**A**), at the ventricles (**B**), below the ventricles (**C**), and bifrontal (**D**).

TABLE 1: Patient demographic and clinical characteristics

Characteristic	Value*
median age (yrs)	24 (19–46)
male sex	33 (100)
type of injury	
blast penetrating	29 (88)
gunshot wound	4 (12)
type of decompression	
bifrontal	19 (58)
bihemispheric	8 (24)
supra- & infratentorial	6 (18)
location of injury	
bifrontal	16 (48)
ventricular	7 (21)
below the ventricle	7 (21)
above the ventricle	3 (9)
median initial GCS score	5 (3–14)
median length of follow-up (mos)	
survivors	34 (6–69)
deaths	2 (<1–10)

* Median values are presented with their ranges in parentheses. All other values represent the number of patients with percentages in parentheses.

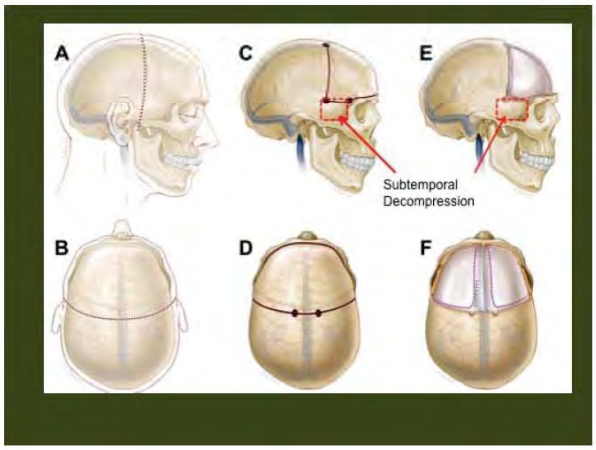
TABLE 2: Association of clinical characteristics and GOS score at 6 months and 1–5 years

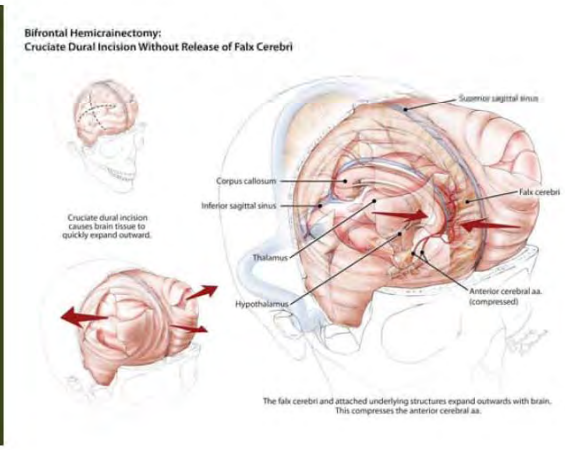
Characteristic	GOS Score at 6 Mos No. of Patients (%) Poor Outcome (Score 1–3)	Good Outcome (Score 4 or 5)	p Value*	GOS Score at 1–5 Yrs No. of Patients (%) Poor Outcome (Score 1–3)	Good Outcome (Score 4 or 5)	p Value*
no. of patients	16	17		12	18	
timing			0.10			0.36
delayed	0 (0)	3 (18)		0 (0)	2 (11)	
early	16 (100)	14 (82)		12 (100)	16 (89)	
focus of initial injury			0.0093			0.0012
bifrontal	4 (25)	12 (71)		2 (17)	13 (72)	
all other locations	12 (75)	5 (29)		10 (83)	5 (28)	
type of decompression			0.27			0.096
bifrontal	8 (50)	11 (65)		5 (42)	12 (67)	
bihemispheric	5 (31)	3 (18)		5 (42)	3 (17)	
supra- & infratentorial	3 (19)	3 (18)		2 (17)	3 (17)	
category			0.21			0.99
gunshot wound	1 (6)	3 (18)		0 (0)	1 (6)	
penetrating head injury	15 (94)	14 (82)		12 (100)	17 (94)	
mechanism of injury			0.92			0.54
blast	8 (50)	9 (53)		6 (50)	11 (61)	
projectile	8 (50)	8 (47)		6 (50)	7 (39)	
presence of						
CSF leak	1/14 (7)	5 (29)	0.26	1/10 (10)	4 (22)	0.082
pulmonary embolism	1/15 (7)	3 (18)	0.26	0/11 (0)	2 (11)	0.36
seizure	6 (38)	5 (29)	0.80	6 (50)	5 (28)	0.45
CNS infection	6/15 (40)	6 (35)	0.87	4/11 (36)	7 (39)	0.66
systemic infection	12/14 (86)	8/16 (50)	0.011	9/10 (90)	11/17 (65)	0.041
ophthalmic injury	5/14 (36)	5 (29)	0.47	3/10 (30)	6 (33)	0.99
pseudoaneurysm	3/15 (20)	4 (24)	0.83	3/11 (27)	4 (22)	0.57
vasospasm	4/15 (27)	6/16 (38)	0.99	5/11 (45)	5/17 (29)	0.63
active cooling	8/10 (80)	10/10 (100)	0.54	6/8 (75)	9/9 (100)	0.29
shunt	5/12 (42)	10/13 (77)	0.17	3/7 (43)	11/15 (73)	0.42
major vascular occlusion	3/14 (21)	0 (0)	0.15	2/11 (18)	0/17 (0)	0.19
any vascular injury	10 (62)	6 (35)	0.039	10 (83)	5 (28)	0.071

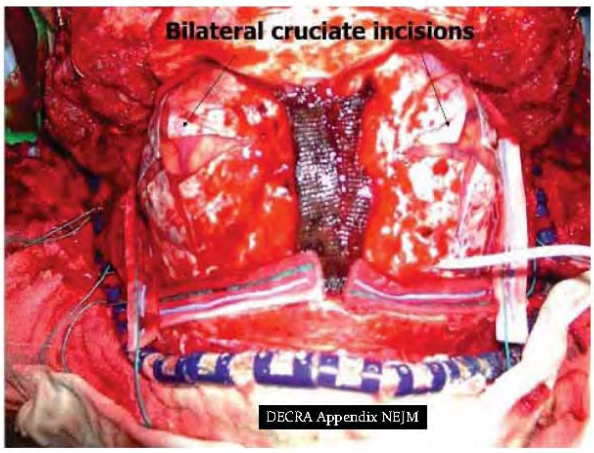
* Probability values were obtained using the Wilcoxon rank-sum test or Kruskal-Wallis ANOVA to compare clinical factors with the numerical GOS outcomes at 6 months and 1–5 years.

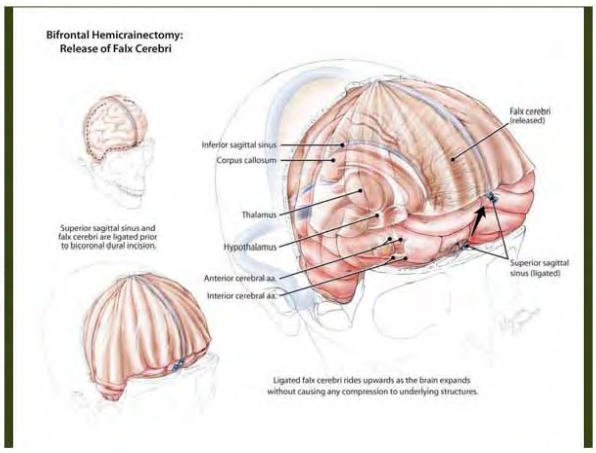
Follow-up Outcome: Military Multi-compartmental

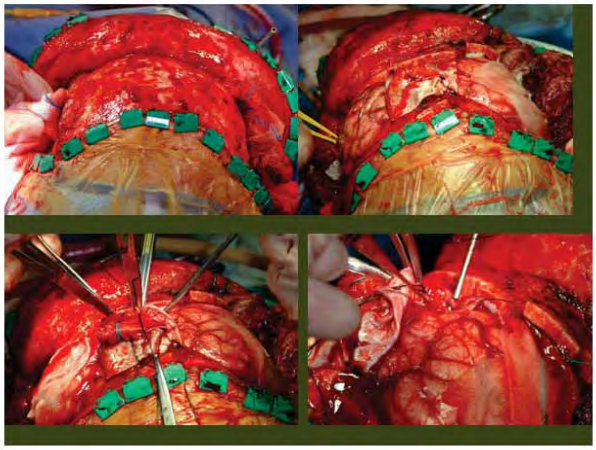
- 33 patients 6 months
- 30 patients 1-5 years
  - 23% dead
  - 17% GOS 2 or 3 (7% vegetative, 10% Dependent)
  - 60% GOS 4 or 5
  - Average > than 2 years (Median 3.4 months Follow-up)

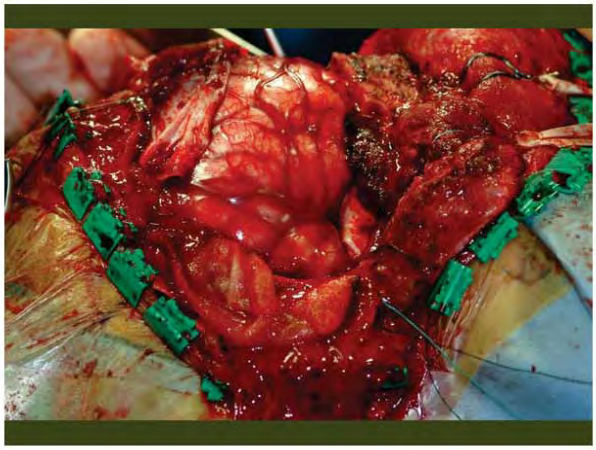


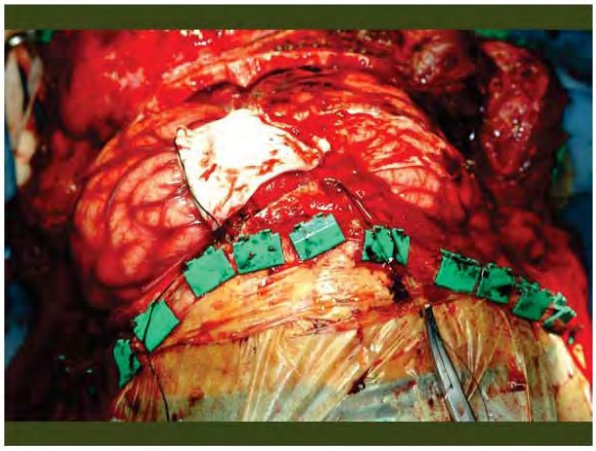


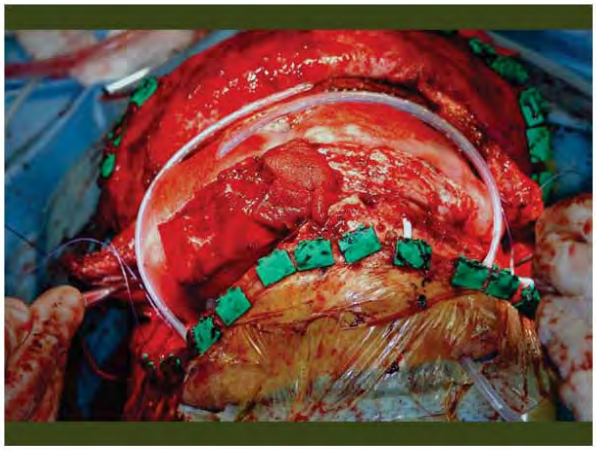

Bilateral cruciate incisions
DECRA Appendix NEJM

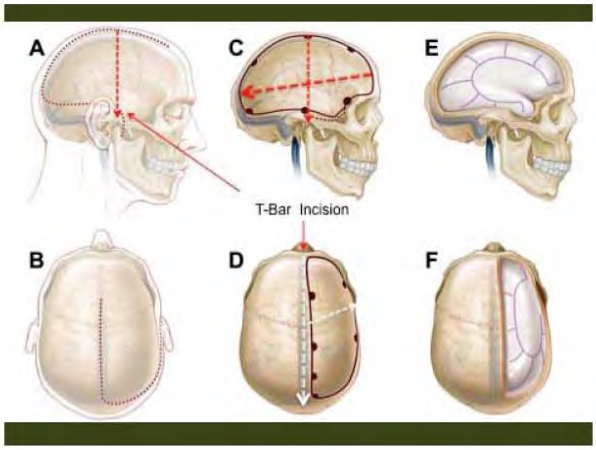

Bifrontal Hemicrainectomy:
Release of Falx Cerebri
Falx cerebri (released)
Inferior sagittal sinus
Corpus callosum
Thalamus
Hypothalamus
Anterior cerebral aa.
Interior cerebral aa.
Superior sagittal sinus (ligated)
Superior sagittal sinus and falx cerebri are ligated prior to bicoronal dural incision.
Ligated falx cerebri rides upwards as the brain expands without causing any compression to underlying structures.





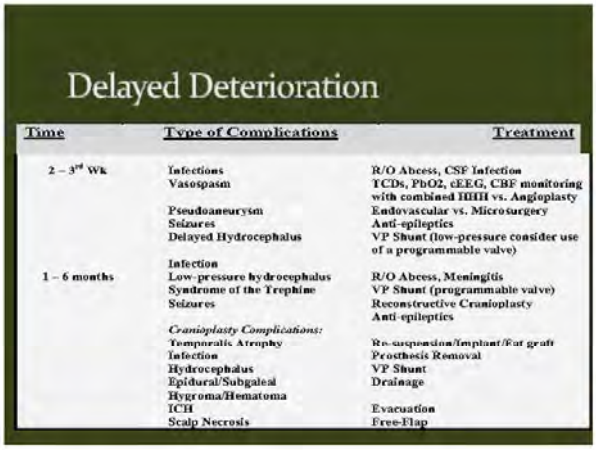




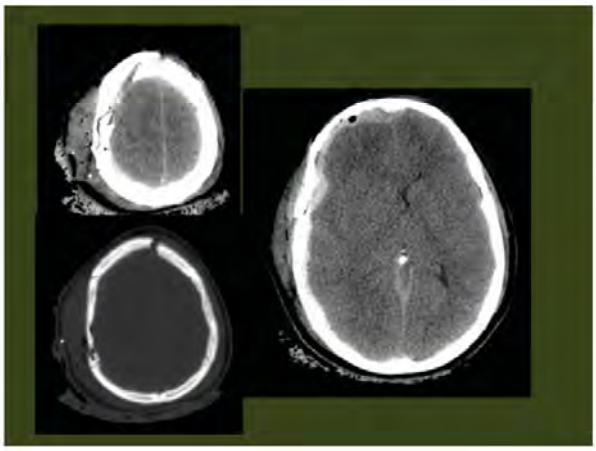


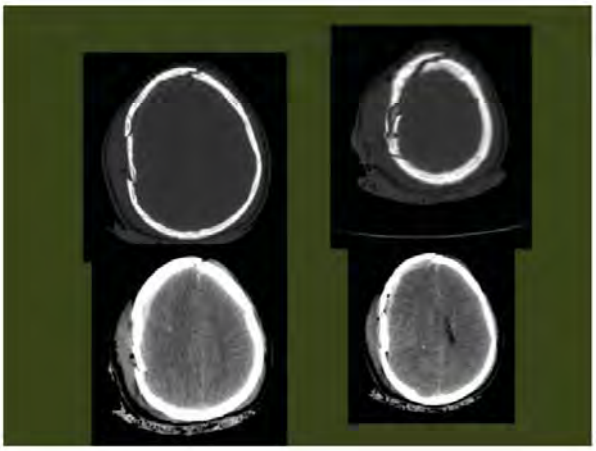
Immediate Complications

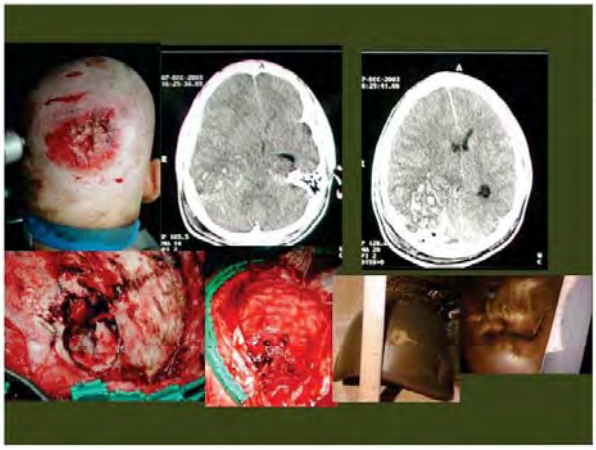
Time	Type of Complications	Treatment
0 – 24 hrs	ICP Increased Hematoma Ischemia Anatomic Defect Hypoxia Hypotension	Hemicraniectomy Evac/Coag Correction Decompression/ID Occlusion Anatomic Closure Airway/Pulmonary Correction Overt or Occult EBL PRBC/FFP/PLTS vs. whole blood vs. Hypertonic Saline
24 – 48 hrs	ICP Increased Hematoma Hydrocephalus Edema Seizure	Hemicraniectomy Evac/Coag Correction Ventriculostomy Decompression Anti-epileptics/cEEG monitoring

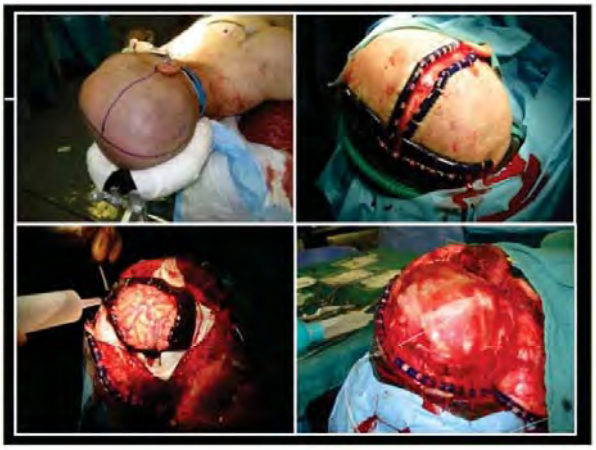

Delayed Deterioration
Time
Type of Complications
Treatment
2 – 3rd Wk
Infections
R/O Abcess, CSF Infection
Vasospasm
TCDs, PbO2, cEEG, CBF monitoring with combined HHH vs. Angioplasty
Pseudoaneurysm
Endovascular vs. Microsurgery
Seizures
Anti-epileptics
Delayed Hydrocephalus
VP Shunt (low-pressure consider use of a programmable valve)
Infection
1 – 6 months
Low-pressure hydrocephalus
R/O Abcess, Meningitis
Syndrome of the Trephine
VP Shunt (programmable valve)
Seizures
Reconstructive Cranioplasty
Anti-epileptics
Cranioplasty Complications:
Temporalis Atrophy
Re-suspension/Implant/Fat graft
Infection
Prosthesis Removal
Hydrocephalus
VP Shunt
Epidural/Subgaleal Hygroma/Hematoma
Drainage
ICH
Evacuation
Scalp Necrosis
Free-Flap

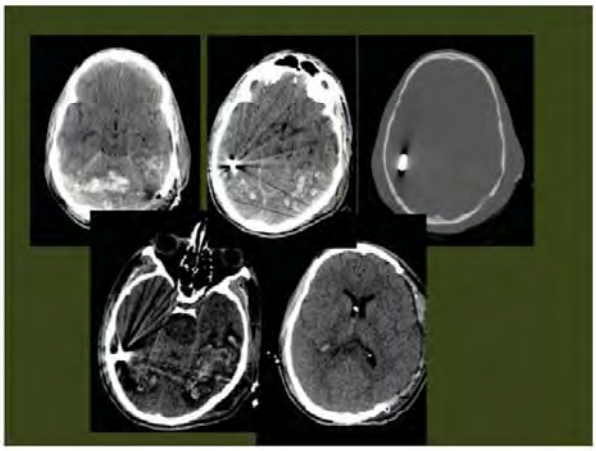

Exit Wound

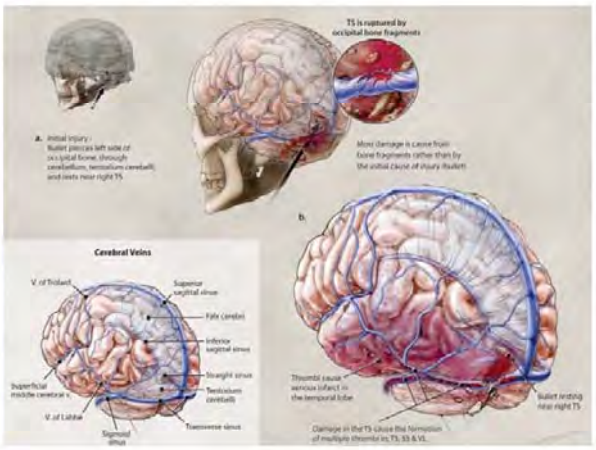











T5 is ruptured by occipital bone fragments
Cerebral Veins

Prophylactic Surgery?
Intractable ICP???

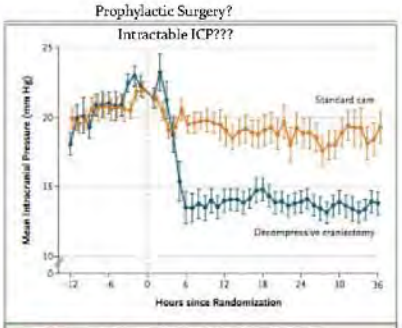


Figure 1. Intracranial Pressure before and after Randomization.
Shown are the mean measurements of intracranial pressure in the two study groups during the 12 hours before and the 36 hours after randomization. The I bars indicate standard errors.

Unbalanced Groups

Table 1. (Continued.)

Characteristic	Decompressive Craniectomy (N = 73)	Standard Care (N = 82)	P Value†
Time from injury to hospital — hr			0.90
Median	1.0	1.2	
Interquartile range	0.8–1.8	0.7–1.9	
Time from injury to randomization — hr			0.60
Median	35.2	34.8	
Interquartile range	23.3–52.8	25.8–45.4	
Marshall class — no. (%)††			0.39
Diffuse injury II	17 (23)	27 (33)	
Diffuse injury III or IV	53 (73)	53 (65)	
Nonevacuated mass lesion (V)	3 (4)	2 (2)	

L. F. Marshall, *et al.*

TABLE 2

*Outcome at discharge in relation to intracranial diagnosis**

Outcome at Discharge	Diffuse Injury I		Diffuse Injury II		Diffuse Injury III		Diffuse Injury IV		Evacuated Mass		Nonevacuated Mass		Brain Stem Injury		Unknown		Totals	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
good	14	27.0	15	8.3	5	3.3	1	3.1	14	5.1	1	2.8	0	0	0	0	50	7.0
moderate	18	34.6	40	26.0	20	13.1	1	3.1	49	17.7	3	8.3	0	0	1	5.9	138	19.5
severe	10	19.2	72	46.7	41	26.8	6	18.8	72	26.1	7	19.4	1	33.3	0	0	209	29.0
vegetative	5	9.6	25	11.3	35	22.9	6	18.8	34	12.3	6	16.7	0	0	0	0	106	14.8
dead	5	9.6	24	15.5	52	34.0	18	56.2	107	38.8	19	52.8	2	66.7	16	94.1	243	32.5
totals	52	100	177	100	153	100	32	100	276	100	36	100	3	100	17	100	746	100

* Outcome classified by the Glasgow Outcome Scale.* For a description of Diffuse Injury I or IV, see Table 1.

Diffuse I Death 9.6%
Diffuse II Death 13.5%
Diffuse III Death 34%
Diffuse IV Death 56.2%

27% NON-RX

12% NON-RX

Pronostic Factors in TBI TRIALS

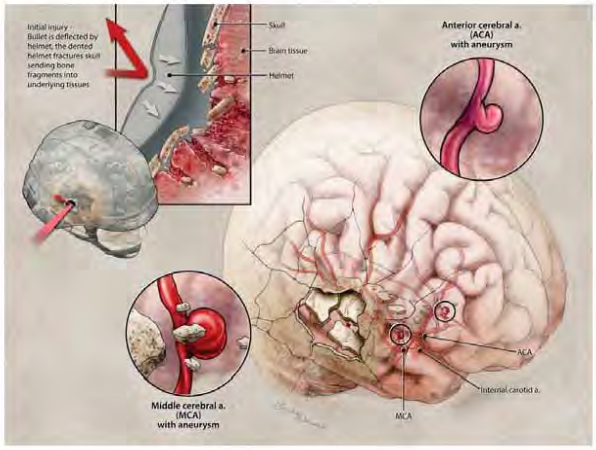
- AGE
- Motor SCORE
- Pupillary Reactivity
  - 3x More Likelihood for Poor outcome when absent
  - IMPACT Trial (Steyerberg PloSMedicine, 2008)
- Marshall Score
  - Grade III Score Worse OUTCOME compared with GdII

INTERIM CHANGE IN STATS?

- INITIALLY 4 OUTCOME SCALE (GOS)
- CHANGED TO 8 OUTCOME SCALE (GOSe)
- INITIALLY REQUIRED 210 PATIENT THEN CHANGED TO 150? AFTER REVIEW OF INTERIM RESULTS
- 15 patients (18%) crossed from the medical to surgical group (analyzed as an intention to treat with their original group).

Mechanism Differences

- Wartime Trauma
  - Heterogenous
  - PBI/Blast/Blunt
  - Concommitant Injuries
  - Skull Base/Maxillofacial Injuries
- DECRA
  - Homogenous
  - Blunt Force (MVA/Falls)
  - Isolated Head
  - No PBI/Blast



Timing of Surgery

- Wartime
  - 90% First 12 hours
  - Unable to monitor ideally during transport
  - Late Swelling that Persists
  - Majority cistern obliteration at Presentation
  - Open Depressed Skull Fractures Required intervention
- DECRA
  - 72 hours Decompression
  - Close Monitoring
  - ICP, >22 mmhg for 15 min
  - Typical Pattern of Swelling Day#3
  - Non-responsive to Maximal Medical Treatment
  - Ventriculostomy?

Differences in Techniques

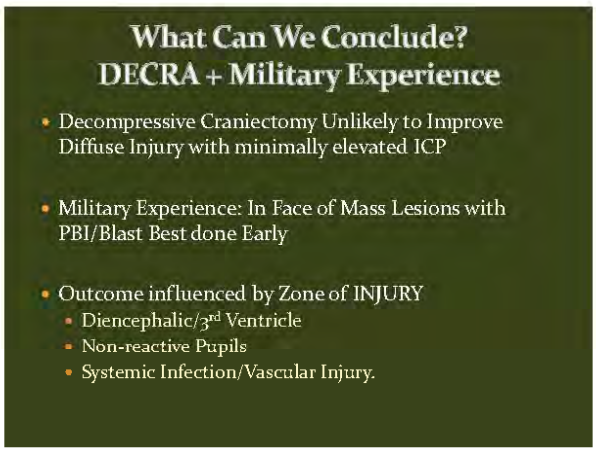
- Wartime
  - Majority 70% Hemicraniectomy
  - Multi-compartmental (30%)
  - Bifrontal 20% with sectioning of the falx
- DECRA
  - All Bifrontal
  - Falx Not Released
  - Bilateral Durotomies

Military Multi-compartmental

- Average Age 24
- Initial GCS 5
- Criteria Significant for Poor Outcome
  - Focus of Initial Injury (3rd vent worse)
  - Any Vascular Injury
  - Systemic Infection
  - GCS 3 @ Conus

CONCLUSIONS: PROBLEMS w/DECRA

- DECRA limited to diffuse injury not mass lesions
  - <5 % of all Patients Screened
- DECRA Shorter follow-up
  - 6months not reflective of Final Outcome
- Higher Percentage w/ non-reactive pupils in Surgical Group (Significant Poor Prognostic Indicator)
- Falx Not Sectioned for Bifrontal Release
- Bifrontal Decompression Likely to have higher complications (<30% of Military Cohort)
- Definition of Elevated ICP ?


What Can We Conclude?
DECRA + Military Experience
Decompressive Craniectomy Unlikely to Improve Diffuse Injury with minimally elevated ICP
Military Experience: In Face of Mass Lesions with PBI/Blast Best done Early
Outcome influenced by Zone of INJURY
Diencephalic/3rd Ventricle
Non-reactive Pupils
Systemic Infection/Vascular Injury.

Treatment with Ethanol Decreases Systemic Inflammation and Improves Functional Recovery After Traumatic Brain Injury in Mice

711 HPW/USAFSAM-ETS

Dr. Timothy Pritts

INTRODUCTION: Traumatic brain injury (TBI) is a major cause of morbidity and mortality in both military and civilian casualties. Clinical studies have suggested that moderate intoxication at the time of head injury is correlated with improved outcome. Previous studies indicate that ethanol attenuates the neuroinflammatory response to traumatic brain injury in mice and may decrease secondary brain injury. We hypothesized that ethanol given after traumatic brain injury would attenuate the neuroinflammatory response and improve functional outcome. METHODS: Mice were subjected to a moderately severe blunt TBI by weight drop or sham injury. At 30 min post injury, mice were given 5 g/kg of ethanol or water by gavage. Serum and brain samples were analyzed for inflammatory cytokines by ELISA. Neuron-specific enolase (NSE) was measured as a serum biomarker of TBI severity. Functional recovery was tested on the rotarod device at intervals up to 2 weeks post injury. RESULTS: In mice receiving ethanol, there were decreased serum levels of KC (145.1 vs. 317.2 pg/mL; $p<0.05$) and IL-6 (57.6 vs. 230.2 pg/mL; $p<0.05$) 3 hr after TBI as compared to those mice receiving vehicle. Serum levels of NSE were diminished in mice receiving ethanol as compared to water (65.6 vs. 164 µg/L; $p<0.05$). Functional recovery, as measured rotarod time, was improved at 3 days after injury in mice receiving ethanol as compared to water (99.7% vs. 36.6%; $p<0.05$). CONCLUSION: After moderate TBI, ethanol decreases systemic inflammation, NSE, and results in improved functional outcome as measured by the rotarod device.

U.S. AIR FORCE

Treatment with Ethanol Decreases Systemic Inflammation and Improves Functional Recovery After Traumatic Brain Injury in Mice

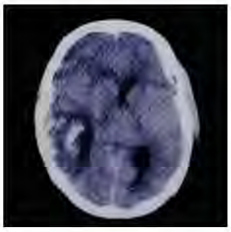
Timothy A. Pritts, MD, PhD
University of Cincinnati

Every Airman a Force Multiplier
August 2011 AFMS Research Symposium

Traumatic Brain Injury (TBI)

Every Airman a Force Multiplier

- Serious cause of morbidity and mortality
- 52,000 civilian deaths
- 80,000 permanent severe neurologic disabilities



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Traumatic Brain Injury

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- Diverse clinical condition
  - Wide range of severity
    - Mild to fatal
  - Various mechanisms of injury
    - Penetrating versus blunt
  - Localization of injury
    - Focal versus diffuse

 3

Secondary Brain Injury

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- Occurs minutes to days after insult
- Related to decreased cerebral oxygenation
  - Hypotension, hypoxia, and increased intracranial pressure
- Neuroinflammation plays an important role in secondary brain injury

 4

Neuroinflammation

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- Cytokines not routinely present in normal, uninjured brain tissue
- Cytokine levels increase rapidly after TBI
  - Inflammatory cell recruitment and activation
  - Increased blood brain barrier permeability

Ethanol

Every Airman a Force Multiplier

- High prevalence among trauma victims
- Modulates the inflammatory response
- Clinical studies investigating ethanol and traumatic brain injury have shown a potential decrease in mortality attributable to ethanol

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First Author	Year	# of Patients	Mortality Outcomes
Alexander	2004	80	No difference
Tien	2006	3675	↓ in moderate EtOH ↑ in high EtOH
Salim	2009	482	↓ in EtOH group
Salim	2009	38,019	↓ in EtOH group
Shandro	2009	836	↓ in EtOH groups (trend)

Previous Work

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- Pretreatment with EtOH:
  - Decreased systemic chemokines
  - Decreased neuroinflammation

Hypothesis

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Treatment with ethanol after experimental TBI would attenuate the neuroinflammatory response.

TBI Model

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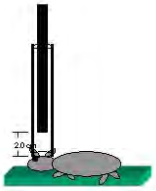

Blunt

Moderate/Concussive

Post-TBI Rapid Righting Reflex

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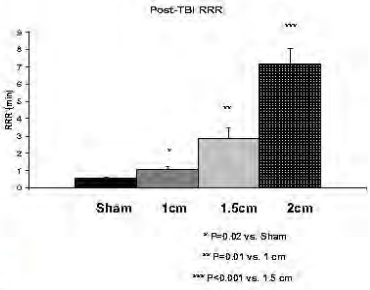

Experimental Design

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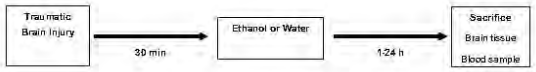

Blood Ethanol Levels

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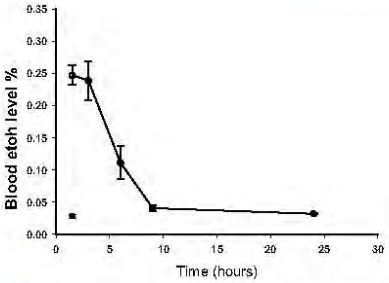

Rapid Righting Reflex

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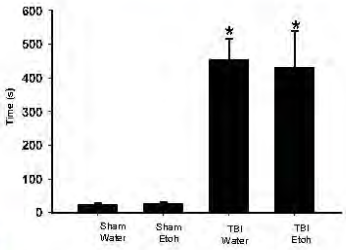

Serum KC

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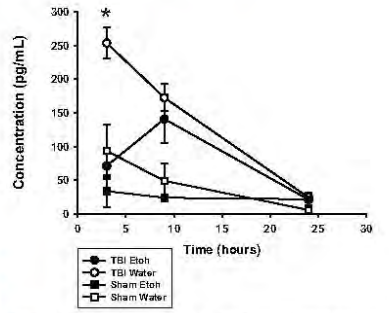

Serum IL-6

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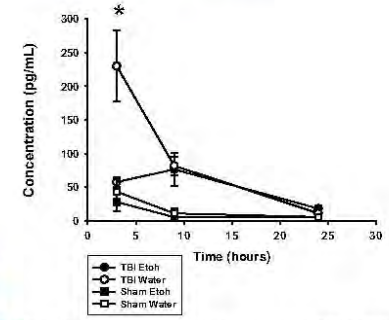
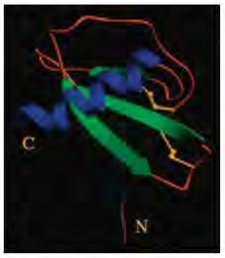


MIP-1α

Every Airman a Force Multiplier

- CCL3
- Proinflammatory cytokine
- Important recruiter and activator of leukocytes
- Shown to be significantly upregulated after TBI



Cerebral MIP-1α

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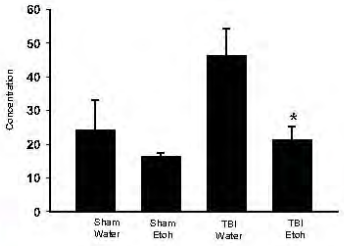

Neuron Specific Enolase

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- Cytoplasmic glycolytic enzyme found in neurons
- Released into serum after TBI
- Correlates with outcome in moderate and severe TBI

Neuron Specific Enolase

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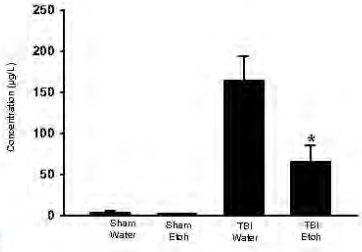

Functional Effects?

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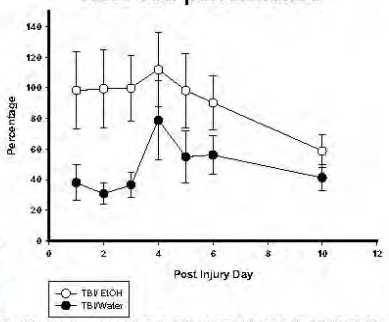
Roto-rod performance



Summary

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- Post-TBI alcohol administration:
  - Decreases serum KC and IL-6
  - Reduces brain MIP-1α
  - Decreases serum neuron specific enolase
  - Improves functional motor performance

Conclusion

Every Airman a Force Multiplier

Ethanol may mitigate the proinflammatory response when given after TBI

Acknowledgments

Every Airman a Force Multiplier

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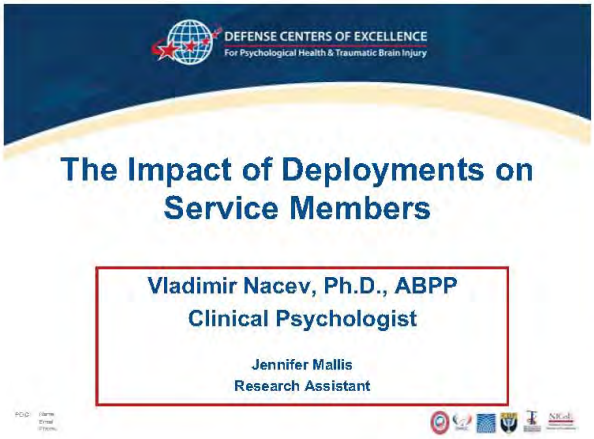
Alex B. Lentsch, PhD

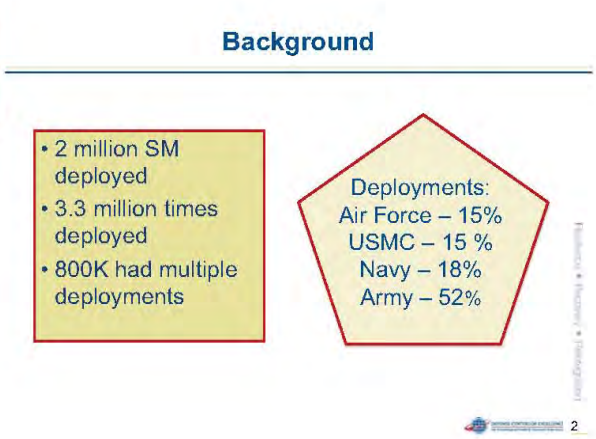
Impacts of Frequent and Multiple Deployments on Substance Abuse by Service Members

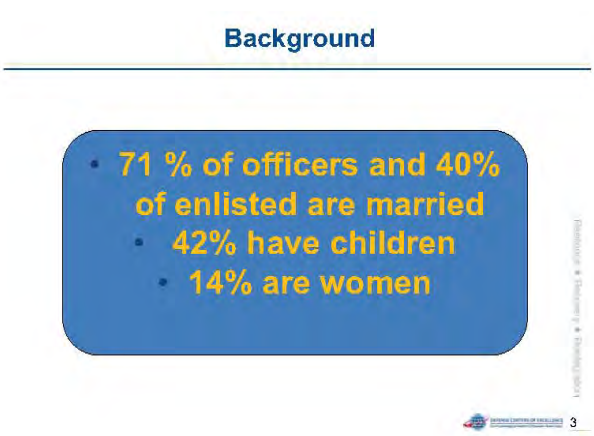
TMA/DCOE

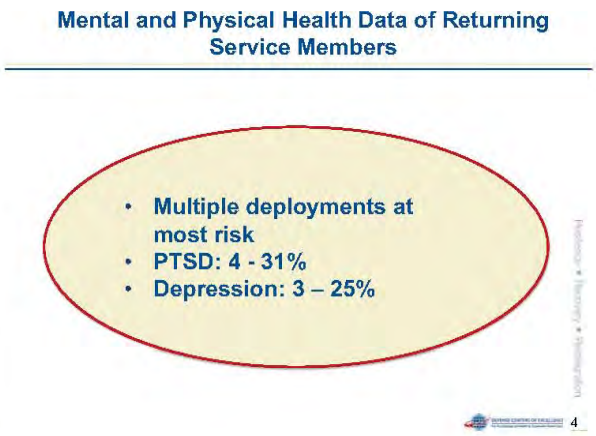
Dr. Vladimir Nacev

As troops return from Iraq and Afghanistan to civilian life, clinicians and policy decision-makers are grappling with how best to address the post-deployment adjustment problems. Data suggest the presence of mental health problems for service members that include posttraumatic stress disorder (PTSD), head injury, interpersonal violence, and substance abuse. Moderate correlations were found between PTSD symptoms severity, substance use, and adverse health outcomes. Regarding substance abuse, problems with alcohol and nicotine abuse are most prevalent and pose a significant risk to the health of veterans as well as the troops in the Reserve Component and National Guard. At greatest risk are deployed personnel with combat exposures, as they are more apt to engage in new-onset of heavy weekly drinking and binge drinking and to suffer alcohol-related problems as well as smoking initiation and relapse. A maximally effective substance abuse prevention program will require layering of interventions across various environments at the DOD/ Services level, installations level, and service members' level. Prevention efforts for heavy alcohol use are likely to be the most productive if they focus on lower- and midgrade enlisted personnel, as the rate for heavy drinkers was nearly twice as high for personnel in the lower pay grades than the higher. Specifically, among young adults, social motives appear to be associated with moderate alcohol use, enhancement with heavy drinking, and coping motives with alcohol-related problems.


DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury
The Impact of Deployments on Service Members
Vladimir Nacev, Ph.D., ABPP
Clinical Psychologist
Jennifer Mallis
Research Assistant


Background
• 2 million SM deployed
• 3.3 million times deployed
• 800K had multiple deployments
Deployments:
Air Force – 15%
USMC – 15 %
Navy – 18%
Army – 52%
2


Background
• 71 % of officers and 40% of enlisted are married
• 42% have children
• 14% are women
3


Mental and Physical Health Data of Returning Service Members
• Multiple deployments at most risk
• PTSD: 4 - 31%
• Depression: 3 – 25%
4

Mental Health Problems - Army

- 1 deployment – 12%
- 2 deployments – 18%
- 3 + deployments – 27%
- 27% active duty
- NG/RC – 35.5%

- Soldiers deployed since 2003:
  - 38% deployed more than once
  - 10% deployed 3 or more times

5

Heavy Drinkers

- Increased risk for injuries
- Decreased overall health and productivity
- Decreased readiness and negative impact on the unit
- Interpersonal problems
- Alcohol dependence

6

Substance Abuse

- Those with PTSD and depression at increased odds for new-onset and continued alcohol related problems
- Reserve/Guard – increased odds for new onset for all 3 drinking outcomes compared to non-deployed

7

Substance Abuse – 2008

- 20% of SM compared to 14% of civilians were heavy alcohol users
- Exposure to combat stress → substance use
- Young SM, RC, NG exposed to combat → greater likelihood for new-onset weekly drinking, heavy episode drinking, and alcohol related problems

8

Alcohol and Deployment Problems – Iraq

- 18-24 y/o more likely to screen positive and less likely to be married
- Significantly more mental health problems
- More combat experiences
- 25% of Soldiers screened positive 4 months following deployment

9

Addressing Alcohol Misuse

- Discourage alcohol abuse – not consistent with readiness
- Promote "That Guy" (www.thatguy.com)
- Increase use of breathalyzers
- Training and education of all personnel
- Promulgate the DOD/VA clinical practice guidelines for substance use disorders

10

Stages of Deployment

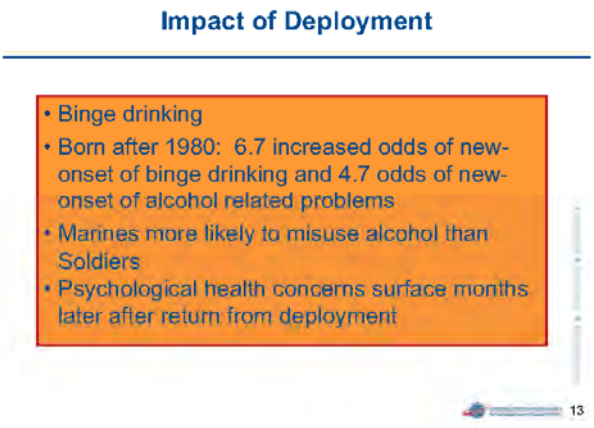
1. Pre-deployment
2. Deployment
3. Sustainment
4. Redeployment
5. Post-deployment

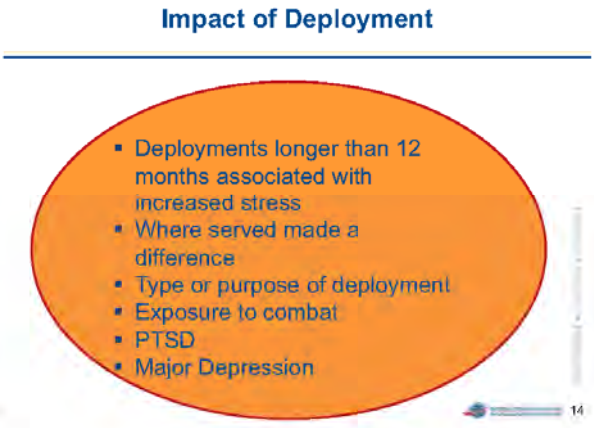
11

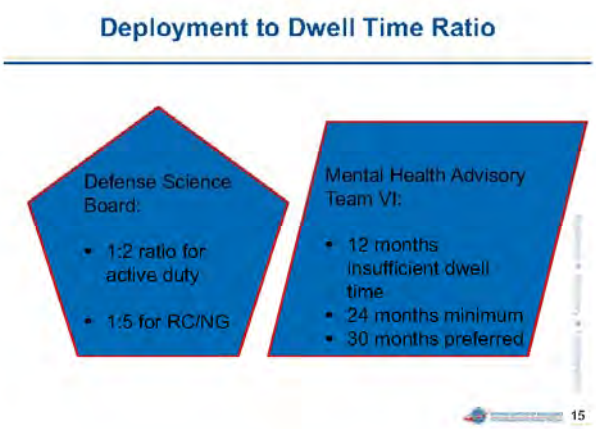
Impact of Combat Exposure

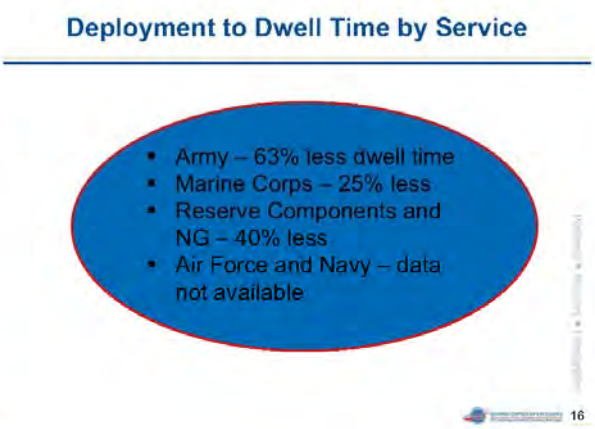
- **Deployed 3 or 4 times** – increased risk for behavioral health problems … alcohol
- **Alcohol misuse**: new on-set of heavy weekly drinking, binge drinking, or alcohol related problems
- **Women** – 1.2 times more likely to report new-onset of heavy drinking; less likely for binge drinking or alcohol related problems
- **Men**: 1.3 times more likely to experience new onset of binge drinking

12


Impact of Deployment
• Binge drinking
• Born after 1980: 6.7 increased odds of new-onset of binge drinking and 4.7 odds of new-onset of alcohol related problems
• Marines more likely to misuse alcohol than Soldiers
• Psychological health concerns surface months later after return from deployment
13


Impact of Deployment
• Deployments longer than 12 months associated with increased stress
• Where served made a difference
• Type or purpose of deployment
• Exposure to combat
• PTSD
• Major Depression
14


Deployment to Dwell Time Ratio
Defense Science Board:
• 1:2 ratio for active duty
• 1:5 for RC/NG
Mental Health Advisory Team VI:
• 12 months insufficient dwell time
• 24 months minimum
• 30 months preferred
15


Deployment to Dwell Time by Service
• Army – 63% less dwell time
• Marine Corps – 25% less
• Reserve Components and NG – 40% less
• Air Force and Navy – data not available
16

Impact on Readiness

- Longer deployments and shorter dwell time → psychological distress
- The rate of psychological problems tends to rise with the number of deployments
- First deployment is most distressing
- Dwell time is less restful if deployment time is unknown
- Initial weeks upon return from deployment is more important than total dwell time

Resilience ★ Recovery ★ Reintegration

17

Addressing Stigma

- Real Warriors Campaign
- Changes to security questionnaire
- CJCS initiative on stigma reduction
- Service wide programs on addressing stigma

Resilience ★ Recovery ★ Reintegration

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Addressing Stigma

Air Force:

- The Suicide Prevention Program, Frontline Supervisor Training, and Wingman Day training, all include stigma-reduction messages.
- Comprehensive Airman Fitness (CAF) makes Airmen aware of helping resources and encourages good wingmanship and responsible help-seeking through semi-annual Wingman Days.

Resilience ★ Recovery ★ Reintegration

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Addressing Stigma

Army:

- Comprehensive Soldier Fitness (CSF) designed to build resilience and enhance performance

Navy *and* ***Marine Corps***:

- The Combat and Operational Stress Control (COSC) provides Navy and Marine Corps leaders guidance on combat and operational stress control

Resilience ★ Recovery ★ Reintegration

20

Questions

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Spouse Abuse and Combat-Related Deployments in Air Force Couples

AFMOA

Maj Rachel Foster

PURPOSE: Despite the general belief that combat-related deployment is associated with increased spousal aggression, evidence showing a link between spouse abuse and deployment is weak. The purpose of this study was to conduct the first population-based investigation comparing rates of spouse abuse among married active duty Air Force (AF) personnel and their spouses after versus before combat-related deployment.

Methods: The sample included all married AF members with at least one substantiated incident of spousal physical or emotional abuse and at least one combat-related deployment between October 1, 2001 and October 31, 2008. Department of Defense (DoD) guidelines regarding the mandatory reporting of spouse abuse by active duty members and DoD civilians changed in April of 2006 to include intimate partners. Substantiated cases of intimate partner violence were deleted from this study so as not to conflate intimate partner violence and spouse abuse. During the 85-month study period, 6,063 individuals in 4,874 AF married couples were reported for 7,003 unique incidents of spouse abuse across 9,676,517 days at risk (i.e., days when neither spouse was deployed).

RESULTS: Overall, spouse abuse rates were lower after deployment (RR = .87, CI95%: .84, .91). This general pattern was found regardless of offender military status, type of abuse, total number of deployments, and total deployment duration. However, in some circumstances spouse abuse rates were higher after than before deployment. For example, for couples exhibiting unidirectional abuse (by either spouse) when the offender had used alcohol, post deployment abuse was higher. Further, for couples in which the husband perpetrated unilateral moderate or severe spouse abuse and used alcohol, the abuse rate was 37% higher after as compared to before deployment. IMPLICATIONS: Although spouse abuse rates increased following deployment under some conditions, the overall rate was lower after deployment. However, because the present study included only abusive couples who had experienced combat-related deployment, these results do not necessarily reflect changes in rates of spouse abuse in the general AF population during the study period. Notwithstanding, the data suggest that prevention efforts should focus not just on spousal violence but also on context and in particular on the use of alcohol.

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Spouse Abuse and Combat-Related Deployments

Brief for the 2011 AFMS Medical Research Symposium, 2 Aug 2011

Maj Rachel E. Foster
Medical Services Flight Commander
Clinical Social Worker, Ph.D.
579th MDG

Research Funding & Contributors

- Project Funding: Air Force Family Advocacy Program
- Air Force Contributors: Lt Col David J. Linkh and Lt Col Carol M. Copeland
- Northern Illinois University Contributors – Center for the Study of Family Violence and Sexual Assault: Joel S. Milner, Ph.D., Mandy M. Rabenhorst, Ph.D., Cynthia J. Thomsen, Ph.D.

Previous Research with Active Duty: Deployment and Spouse Maltreatment

- Three studies of married Army personnel
  - Male perpetrated physical spouse abuse only
  - Between-groups design (deployed vs. not)
  - Troops were deployed in support of a peace-keeping mission in Bosnia
  - Excluded dual military
- Summary of Results:
  - One study: Longer deployments were (weakly) associated with increased likelihood of severe, but not moderate, spouse abuse
  - Other two studies: No difference in spouse abuse between deploying and nondeploying families
    - Either pre- or post-deployment
    - Whether reported by the husband or wife

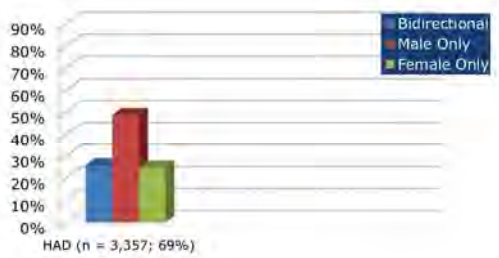
Combat Deployment and Spouse Abuse in AF Couples: Our Study

- Objective: To conduct the first population-based study comparing rates of substantiated physical and/or emotional spouse abuse among married active duty Air Force (AF) personnel and their spouses after versus before combat-related deployment.
- Sample: All married AF personnel and their spouses who have:
  - been involved in at least one substantiated incident of spouse physical or emotional abuse, and
  - experienced at least one combat-related deployment between 1 October 2001 and 31 October 2008

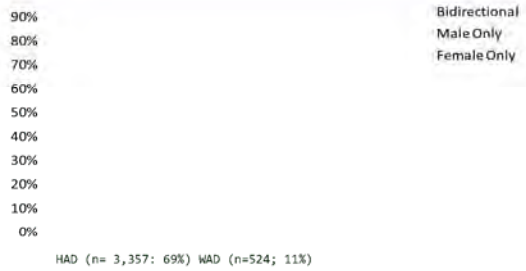
Methods

- Two data sets:
  - Family Advocacy System of Records (AFMOA)
  - Deployment Data (Brooks City-Base, now at Kelly)
- During the 85-month study period, 6,063 individuals in 4,874 AF couples perpetrated 7,003 unique incidents of spouse abuse across 9,676,517 days at risk (i.e., days when neither spouse was deployed).
- Data are organized by couple; each couple was associated with up to:
  - 10 substantiated incidents of abuse (M = 1.44, SD = .78, 47% had more than one) and
  - 9 combat-related deployments (M = 1.89, SD = 1.11, 32% had more than one)

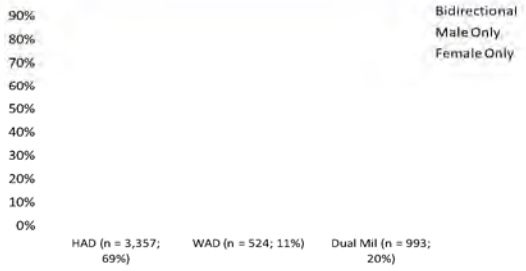
Results - Descriptive



Results - Descriptive



Results - Descriptive



Results

- During the 85-month study period, of the 4,874 AF couples that perpetrated 7,003 unique incidents of spouse abuse across 9,676,517 days
- Military personnel perpetrated the majority (64%) of all incidents
- 25% of couples were involved in bidirectional abuse (82% on the same day)
- Of the 75% with unidirectional abuse, offenders were most often male (71%) and were most often the spouse who deployed (60%)

Results

- Of the 7,003 incidents:
  - 23% involved moderate or severe abuse
  - 22% involved offender alcohol use
  - 6% involved both

Adjusted* Rates of Spouse Abuse

- Poisson regression was used to compare rates of spouse abuse *regardless of timing relative to deployment* stratified by variables of interest
- Adjusted* rates were significantly higher for couples with:
  - Enlisted versus officer
  - Bidirectional versus unidirectional abuse
  - No children vs. with children
  - Physical or both physical and emotional vs. emotional only
  - At least one moderate/severe incident vs. mild only

* Adjusted for all other characteristics

Adjusted Rates of Spouse Abuse

- Adjusted rates did not vary by:
  - Family type (i.e., husband active duty, wife active duty, dual military)
  - Offender military status
  - Offender alcohol use in incident
  - Couple race
  - Number of deployments
  - Deployment duration
- Note: given our select sample, the actual rates we calculated do not reflect rates in the general AF population

Rate Ratios of Spouse Abuse Post- vs. Pre-Deployment

- Conditional Poisson regression was used to compare rates of spouse abuse post- vs. pre-deployment
- Contrary to expectations, overall spouse abuse rates were significantly lower following combat-related deployment than before, $p < .001$
  - RR = .87, $CI_{95\%}$ .84, .91
  - Controlling for the year of the couple's first deployment did not alter this finding; RR = .81

Rate Ratios of Spouse Abuse Post- vs. Pre-Deployment

- Spouse abuse rates were lower following deployment regardless of:
  - Offender military status
  - Abuse type (physical vs. emotional)
  - Couple's race and presence of children
  - Number of deployments
  - Total deployment duration
- This pattern was significant for
  - Husband AD, but not Wife AD or dual military
  - Bidirectional, but not unidirectional abuse
  - Mild, but not moderate/severe incidents
  - Incidents *not* involving offender alcohol use

Rate Ratios of Spouse Abuse Post- vs. Pre-Deployment

- In contrast to the general pattern, rates of spouse abuse were significantly higher following deployment in:
  - unidirectionally violent couples
    - with male perpetrators
      - rates of moderate/severe spouse abuse and/or
      - abuse involving offender alcohol use
- Specifically, the abuse rate among couples in which the husband perpetrated unilateral moderate or severe spouse abuse and used alcohol was 37% higher after than before deployment

Discussion

- Possible explanations for overall post-deployment decreases in rates of spouse abuse:
  - Appreciation for one's spouse or posttraumatic growth following deployment
  - Resiliency initiatives instituted by AF to address deployment-related concerns
  - Post-deployment increases may take longer to appear (cf. Orcutt et al., 2003; Prigerson et al., 2002)
  - Results may reflect pre-deployment increases
- Possible reasons for increases in certain groups:
  - Combat-related deployment related to increased substance use

Future Research

- Time series design that evaulates trends pre- and post deployment trends
- Combat-related deployments and post-traumatic stress indicators

Limitations

- Cannnot account for divorces
  - People entering and leaving the database
- Cannot account for possible pre-deployment increases
- Cannot account for those acts of violence that are never reported to AF Family Advocacy Program

Summary and Questions

Questions?

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DSN 297-0611/Comm 202-767-0611

The Psychometric Properties and Clinical Utility of the Air Force Post-Deployment Health Reassessment (PDHRA) for Airmen with Posttraumatic Stress Disorder (PTSD) or Depression

AFMSA

Maj Michael McCarthy

Operation Enduring Freedom (OEF) (Afghanistan) and Operation Iraqi Freedom (OIF) represent one of the longest wartime deployments in the history of the American military. To date, more than 2 million American military members have deployed. Of these, an estimated 300,000 have returned with a mental health condition, such as depression or PTSD. The Department of Defense has established a robust screening program to identify and track deployment-related physical and psychiatric illnesses. The Post-Deployment Health Reassessment (PDHRA) is a primary tool to identify physical and psychiatric risk following a deployment. The PDHRA is a web-based survey, which is administered between 90-180 days after a deployment. This study seeks to evaluate the psychometric properties and clinical utility of the Post-Deployment Health Reassessment (PDHRA) for accurately identifying truama and depression among Airmen following a deployment. Descriptive statistics, confirmatory factor analysis and structural equation modeling were used to address separate research aims. Study aims assessed the impact of deployment on military members and the clinical utility and psychometric properties of the Post-Deployment Health Reassessment. Findings suggest that the Post-Deployment Health Reassessment is a useful triage tool to identify trauma and depression among Airmen following deployment. The study makes recommendations for improving the clinical utility and psychometric properties of the Post-Deployment Health Reassessment (PDHRA).

Headquarters U.S. Air Force

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The Psychometric Properties and Clinical Utility of the PDHRA for Airmen with PTSD or Depression

Major Michael McCarthy
Air Force Suicide Prevention Program Manager

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1

Problem Statement

- >1.6 million service members deployed since '01
- An estimated 300,000 have returned with a mental health condition, such as depression or PTSD, DoD wide (Rand, 2008)
- The PDHRA is a primary tool to identify returning military members with mental health needs
- Efficacy of the PDHRA at identifying returning military members with mental health needs remains unexamined

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2

Research Aims

- Assess the internal consistency of PDHRA subscales and supplemental assessments
- Assess the sensitivity, specificity, positive predictive value and negative predictive value of the PDHRA for depression and PTSD
- Assess the factor structure of PDHRA questions related to TBI, Depression, Trauma, Alcohol Misuse and Support Network Conflict
- Assess the effect size of various scales and individual PDHRA items on depression and trauma
- Assess the Predictive Validity of the PDHRA for Depression and PTSD
- Identify areas to improve the ability of the PDHRA to identify Airmen at risk for PTSD and Depression

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3

Sample

- N=58,242 (over 99% response rate)
- PDHRA responses and supplemental AUDIT, PHQ-9 and PCL-M from 1 Jan 08- 1 Jan 09
- DSM dx from PDHRA completion date- 1 Dec 09
- 85% male
- Pay grades ranged from Airman Basic (E-1) through Major General (0-8)
- The average respondent in this study had deployed twice *(M=1.98, SD=1.76)*

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Internal Consistency

- Alcohol Screening Questions (α=.60)
- PTSD Screening Questions (α=.76)
- Depression Screening Questions (α=.83)
- AUDIT (α=.93)
- PCL-M (α=.98)
- PHQ-9 (α=.99)

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Supplemental Scales

- AUDIT
  - *M=11.99, SD=5.93*
  - Significantly above the clinical score of 8
  - Approaching the clinical cutoff of 13 for females and 15 for males which is likely to indicate alcohol dependence
- PCL-M
  - *M=6.91, SD=14.08*
  - >3 SD below the PCL-M's clinical cutoff level of 50
- PHQ-9
  - *M=2.10, SD=9.37*
  - <1 SD of mild/moderate clinical concerns range (5/10)

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Sensitivity/Specificity for Depression

		Depression Diagnosis		
		No (Specificity)	Yes (Sensitivity)	Total
PDHRA Behavioral Health Concerns	No	37713 **(65.1%)**	100 (29.6%)	37813 (64.9%)
	Yes	20191 (34.9%)	238 **(70.4%)**	20429 (35.1%)
Total		57904 (100%)	338 (100%)	58242 (100%)

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Sensitivity/Specificity for PTSD

		PTSD Diagnosis		
		No (Specificity)	Yes (Sensitivity)	Total
PDHRA Behavioral Health Concerns	No	37772 **(65.0%)**	41 (25.6%)	37813 (64.9%)
	Yes	20310 (35.0%)	119 **(74.4%)**	20429 (35.1)
Total		58082 (100%)	160 (100%)	58242 (100%)

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Chi-Square/Odds/Likelihood Ratios for Depression

- + PDHRA is significantly associated with depression dx $x^2(1, N=58,242)=186.43$, $p=<.001$
- Depression Dx: + PDHRA= 1 out of 85; - PDHRA= 1 out of 378
- Airmen with + PDHRA >4x likely to be diagnosed with depression

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Chi-Square/Odds/Likelihood for PTSD

- + PDHRA is significantly associated with PTSD dx, $x^2(1, N=58,242)=108.81$, $p=<.001$
- PTSD Dx: + PDHRA= 1 of 171; - PDHRA= 1 of 922
- Airmen with + PDHRA >5x more likely to be diagnosed with PTSD

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Factor Structure

$x^2(76, N=58,242)=1243.05$, $p=<.001$, CFI=.99, TLI=1.00, RMESA=.02.; $p=<.001$

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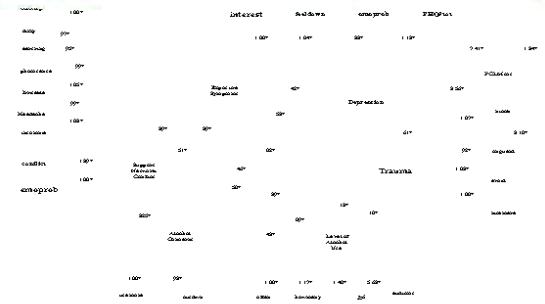
Factor Structure with Supplemental Scales



$x^2(92, N=58,242)=2747.34$, $p=<.001$, CFI=.98, TLI=.99, RMESA=.02; $p=<.001$

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Improving PDHRA Sensitivity/Specificity

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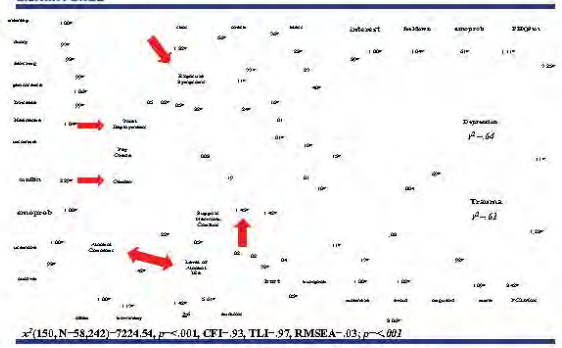

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Predictive Model

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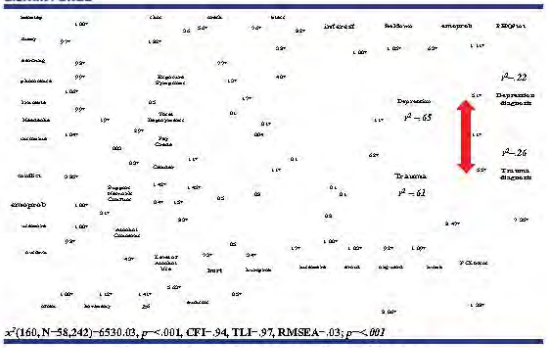

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Continued Use of Supplemental Scales

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- Supplemental Assessments (AUDIT, PCL-M, PHQ-9)
  - Inclusion
    - High α
    - Strong factor loadings
    - Improved CFA model fit
    - Established validity
    - "hurtprob" and "shot"
    - 2 factor solution for alcohol items
  - Exclusion
    - Decreased measurement and path model fit
    - Decreased effect size on diagnostic endogenous variables
    - Parsimony

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PDHRA Areas for Improvement

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- Support Network Conflict
  - Largest effect size
  - Poor operationalization
  - May benefit from inclusion of standardized scale
- Alcohol Variables
  - Poor internal consistency
  - Low sensitivity
  - Limited effects on depression and trauma

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Informative Findings

- Total Deployments
  - Not related to PTSD or depression
    - May suggest shorter deployment cycle is protective
    - Healthy Warrior Phenomenon
    - Post-deployment screening/support
- Pay Grade
  - Related to depression only
  - May suggest that the inclusion of operational stress questions would increase clinical utility

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Informative Findings

- Gender
  - Gender specific thresholds
  - AUDIT scores
- Exposure Symptoms (TBI)
  - Significant direct effects on trauma and depression in measurement and path models
  - Suggests exposure symptoms should be included in PDHRA behavioral health concerns

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Strengths/Limitations

- **Strengths**
  - **Large N**
  - **Use of modeling**
  - **Addressed lit gap**
- **Limitations**
  - **Poor post-PDHRA control**
  - **Exclusion of TBI**
  - **Limited Generalizability**

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Questions?

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Trends in the Early Care of Casualties with Polytrauma and Moderate or Severe TBI

USUHS/GSN (USAF/NC)

Lt Col Karen O'Connell

Moderate and severe traumatic brain injuries (TBIs) result in death or significant lifelong deficits. Secondary insults such as hypovolemic hypotension, hypoxia, and hypothermia exacerbate primary TBI. The purpose of this study was to describe the characteristics of casualties with polytrauma and a moderate or severe TBI. Data from the Joint Theater Trauma Registry for casualties with polytrauma/TBI admitted to a Level III facility were studied. All American forces who sustained blunt trauma with a head Abbreviated Injury Score > 2 and an admission Glasgow Coma Scale score ≤ 12 between 2006 and 2010 were included. Descriptive and bivariate statistics were used to determine any trends in admission vital signs, massive transfusion requirements, or mortality during the first 24 hours after injury. Data were available for 239 casualties. Once admitted to a level III facility, survival was 91.2%, similar to overall casualty survival statistics. Hypoxia and hypothermia occurred in less than 6% of casualties. Hyperthermia and hypotension occurred in 15.9% and 14.6% of casualties, respectively. A massive transfusion was required in 17.6% of casualties. There was a significant correlation between Level III admission vital signs and mortality and the administration of a massive transfusion. The results demonstrate the high incidence of hyperthermia and emphasize the need to closely monitor temperature as uncontrolled hyperthermia may contribute to secondary brain injury. The correlations are not unexpected but warrant further examination of the relationships. Casualties with polytrauma/TBI have a high survival rate revealing the need for further secondary insult prevention research to improve outcome.**These are the preliminary results for a study intended to benchmark 24 hour mortality and evaluate the relationships between the level III facility admission vital signs and 24 hour mortality in this population.

"The author acknowledges Joint Theater Trauma Registry (JTTR) for providing data for this study."

Trends in the Early Care of Casualties with Polytrauma and Moderate to Severe TBI

Karen M. O'Connell, Lt Col, USAF, NC
PhD Student, Graduate School of Nursing
Uniformed Services University of the Health Sciences

Disclaimer

- The views expressed are those of the authors and do not reflect the official policy or position of the Uniformed Services University of the Health Sciences, the Department of Defense, the United Stated Air Force, or the United States government.
- Funding received from Uniformed Service University of the Health Sciences Intramural Funds

Overview

- Background
- Sample Characteristics
- Physiologic Data
- Correlations
- Findings/Implications
- Future Directions
- Summary

Background

- TBI occurs frequently in the current conflicts
- 212,742 from 2001 to 1st quarter 2011
  - 2,235 severe and 35,661 moderate = 37,896
    (DVBIC, 2011)
- Long term deficits may impair survivor's ability to return to work or even care for themselves

Background

- 10 years of ground operations in OIF & OEF
- Joint Theater Trauma Registry (JTTR) a component of the Joint Theater Trauma System was created in 2004
- Data repository to facilitate performance improvement
- JTTR contains demographic, mechanistic, physiologic, and mortality data for all OIF & OEF casualties who arrive at a level III facility

Background

- First time *real time* combat data analyzed to improve care
- Improvements in care seen by implementation of Clinical Practice Guidelines
- Other injury groups have been evaluated
- Little data published on casualties with polytrauma and moderate or severe TBI

Goal

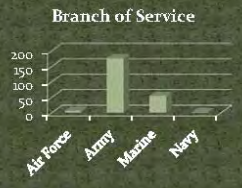
- To develop benchmark metrics to evaluate the effectiveness of the JTTS in improving the care of casualties with combat-related polytrauma and a moderate or severe blunt TBI

Sample

- All American military with a blunt TBI & head AIS ≥ 2 entered in the JTTR between 1 Jan 06 and 31 Dec 10
- 1,680 cases returned
- Limited to those who had a GCS ≤ 12 upon arrival at the level III facility
- Did not limit to isolated TBI
- Final sample 239 cases

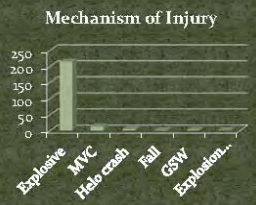
Sample Characteristics

- 97.9% male
- 25.78 years old (mean)
  - Range 18 to 46 years old
- 73.6% Army
- 60.3% OEF
- 38.9% injured in 2010



Sample Characteristics

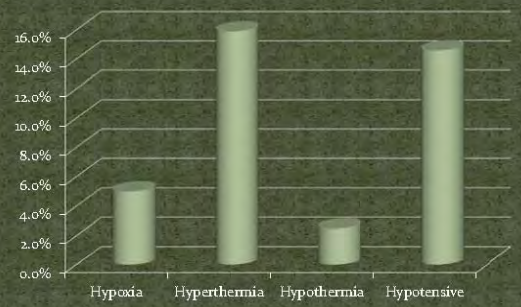
- 90% injured by explosive device
- Military ISS mean 41.15
  - Range 4 – 75



Physiologic Data

- Mean GCS 4.49
  - 76.6% GCS = 3
- 82.8% Sedated on arrival to level III
- 85.8% Intubated on arrival to level III
- 17.6% required a Massive Transfusion
  - ≥ 10 units PRBCs within 1st 24 hours
- 8.8% Mortality within 1st 24 hours

Occurrence of Secondary Insults



Correlations

- Vital Signs – SaO_2, SBP, MAP, HR & Temp
  - Significant correlations between vital signs
  - Strongest correlation between HR & Temp (r=.311)
  - SBP & MAP correlated at r=.884
    - MAP created from SBP
- SaO_2 , SBP, MAP, & HR significant correlation with 24 hour mortality & administration of a massive transfusion
- Administration of a massive transfusion significant correlation with 24 hour mortality (r=.166)
- 19% Mortality after a massive transfusion

Correlations between Vital Signs

	SaO2	SBP	MAP	HR	Temp
SaO2	---				
SBP	.298*	---			
MAP	.287*	.884*	---		
HR	.189*	.036	.033	---	
Temp	.329*	.019	.009	.311*	---
Massive Transfusion	-.173*	-.193*	-.232*	.156*	.030

* Significant at the p ≤.05 level

Correlation with 24 Hour Mortality

	24 Hour Mortality
SaO2	-.340*
SBP	-.319*
MAP	-.266*
HR	-.118
Temp	-.131
Massive Transfusion	.116*

* Significant at the p <.05 level

Findings/Implications

- Data from the JTTR for this population:
  - Demographic data complete
  - Level III data - missing vital signs data: between 0.4% (HR) & 14.2% (temperature)
  - Level II data – missing vital signs data : 56.9% (HR) to 72.8% (temperature)

Findings/Implications

- Mortality among casualties with polytrauma and a moderate or severe TBI, 8.8%, is higher than overall combat mortality rate
  - Eastridge et al (2009) found mortality of 5.2% in sample from July 2003 to July 2008
  - Mason (2007) reported a 4% mortality for casualties treated at Balad AB, Iraq
- Over 90% of these casualties survive
  - Vital to discover effective treatment to improve functional outcomes

Findings/Implications

- Hyperthermia occurs in 15.9% of these casualties
  - 33% of isolated TBI casualties were hyperthermic in first 72 hours (Bridges & Biever, 2010)
- Temperature must be monitored – uncontrolled hyperthermia may contribute to secondary brain injury

Findings/Implications

- 17.6% required a massive transfusion
  - In separate studies Eastridge et al (2009 & 2010) reported rate of massive transfusion to be 6.4 to 6.8%
- Evaluate why the incidence of massive transfusion is higher in this group of casualties

Findings/Implications

- Mortality rate following massive transfusion is over 2 times that of overall mortality for this group of casualties
  - 19% mortality in those who received a massive transfusion in our sample
  - Eastridge et al (2010) reported mortality of 20.8% and Larson (2010) reported mortality of 20% in those receiving massive transfusion
- Evaluate why mortality is higher in these casualties

Limitations

- Retrospective Study
- Data collected under extreme conditions by providers
- 'Snapshot' data – cannot evaluate trends

Future Directions

- Investigate relationship of hyperthermia and outcome
  - 14.2% missing data in this sample restricts the validity of the results
- Investigate relationship between administration of a massive transfusion and 24 hour mortality

Acknowledgements

- The author acknowledges the Joint Theater Trauma Registry (JTTR) for providing the data for this study
- Intramural funding by Uniformed Services University of the Health Sciences
- Dr. Marguerite Littleton-Kearney (Chair), Dr. Sandra Bibb, & Dr. (Col) Elizabeth Bridges – my dissertation committee

Summary

- Background
- Sample Characteristics
- Physiologic Data
- Correlations
- Findings/Implications
- Future Directions
- Summary


Questions?

The Traumatic Brain Injury Research Portfolio of the Army and Defense Medical Research and Development Programs: An Overview

US Army Medical Research and Materiel Command

COL Dallas Hack

The US Army Medical Research and Materiel Command (USAMRMC) has been tasked with the management of Army and Defense Medical Research and Development Program (DMRDP) intra- and extramural projects addressing the diagnosis and treatment of traumatic brain injury (TBI). While these research topics are by no means new to the command, increased funding in response to the significant increase in TBI since the onset of Operations Iraqi Freedom and Enduring Freedom has enabled expansion and expedition of research efforts. As of April 2011 over 450 projects at a cost of over $400M have been awarded or are pending award. These efforts span epidemiology, diagnostics, monitoring, en-route care, initial and definitive treatment, protection and rehabilitation. This large and complex portfolio will be reviewed with respect to promising results and remaining research gaps according to our Continuum of Care model. The project management process involving three Joint Program Committees and their relevant working groups will be described. The goal is for our partners in our sister services to better understand the scope of the portfolio as well as the joint-service nature and processes of portfolio management.

AFMS Medical Research Symposium

TRAUMATIC BRAIN INJURY

DoD Research Overview

COL Dallas C. Hack
Director, Combat Casualty Care Research Program
US Army Medical Research and Materiel Command
Chair, JPC6 & JTCC6 (Combat Casualty Care)
3 August 2011

The views expressed in this presentation are those of the author and do not reflect official policy or position of the Department of the Army, Department of Defense or the U.S. Government.

Briefing Outline

PURPOSE: To provide a broad overview of Traumatic Brain Injury research funded through the Defense Medical Research & Development Program and USAMRMC

1. TBI Research Overview
2. Highlighted Projects
3. Interagency Collaboration

BLUF

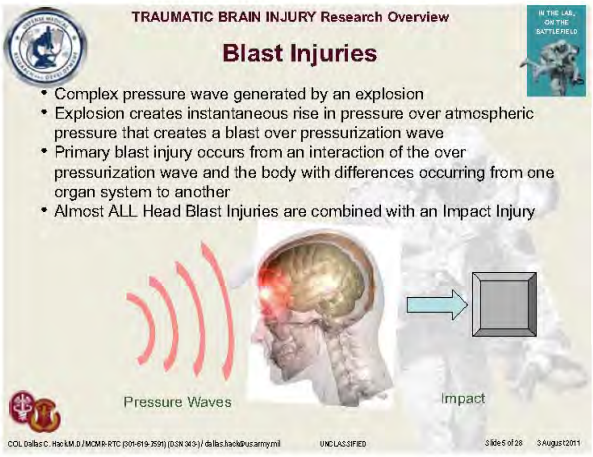
PURPOSE: To provide a broad overview of Traumatic Brain Injury research funded through the Defense Medical Research & Development Program and USAMRMC

1. **No FDA approved objective test for mTBI**
2. **No FDA approved treatment for TBI**
3. **JPC6 is coordinating a comprehensive research approach to this medical frontier**

TBI in the Military

- 1.5 **million** cases and 50,000 deaths each year in the US
- #1 cause of disability for those under the age of 24 years old
- Direct medical costs is over $60 billion in the US each year
- Frequent cause of morbidity and mortality in modern battlefield
- Penetrating brain injuries claim 25% of soldiers killed in battle
- 2/3 of casualties have brain injuries and concussion is growing military medical problem

http://www.brainandspinalcord.org/brain-injury/statistics.html


TRAUMATIC BRAIN INJURY Research Overview
Blast Injuries
• Complex pressure wave generated by an explosion
• Explosion creates instantaneous rise in pressure over atmospheric pressure that creates a blast over pressurization wave
• Primary blast injury occurs from an interaction of the over pressurization wave and the body with differences occurring from one organ system to another
• Almost ALL Head Blast Injuries are combined with an Impact Injury
Pressure Waves
Impact
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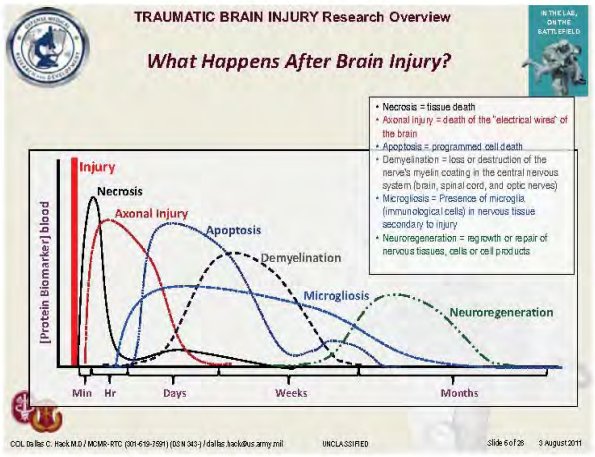
TRAUMATIC BRAIN INJURY Research Overview
What Happens After Brain Injury?
• Necrosis = tissue death
• Axonal injury = death of the "electrical wires" of the brain
• Apoptosis = programmed cell death
• Demyelination = loss or destruction of the nerve's myelin coating in the central nervous system (brain, spinal cord, and optic nerves)
• Microgliosis = Presence of microglia (immunological cells) in nervous tissue secondary to injury
• Neuroregeneration = regrowth or repair of nervous tissues, cells or cell products
[Protein Biomarker] blood
Injury
Necrosis
Axonal Injury
Apoptosis
Demyelination
Microgliosis
Neuroregeneration
Min Hr Days Weeks Months
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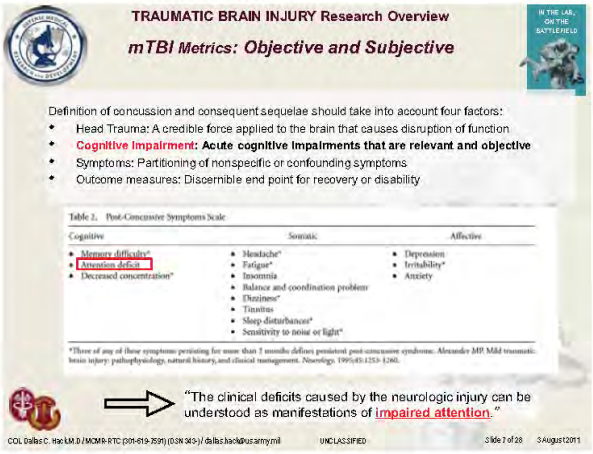
TRAUMATIC BRAIN INJURY Research Overview
mTBI Metrics: Objective and Subjective
Definition of concussion and consequent sequelae should take into account four factors:
• Head Trauma: A credible force applied to the brain that causes disruption of function
• Cognitive Impairment: Acute cognitive impairments that are relevant and objective
• Symptoms: Partitioning of nonspecific or confounding symptoms
• Outcome measures: Discernible end point for recovery or disability
Table 1. Post-Concussive Symptoms Scale
Cognitive
Somatic
Affective
Memory difficulty*
Attention deficit
Decreased concentration*
Headache*
Fatigue*
Insomnia
Balance and coordination problem
Dizziness*
Tinnitus
Sleep disturbances*
Sensitivity to noise or light*
Depression
Irritability*
Anxiety
"The clinical deficits caused by the neurologic injury can be understood as manifestations of impaired attention."
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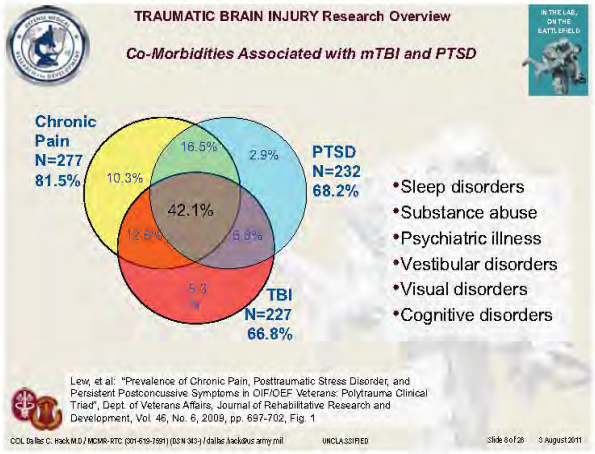
TRAUMATIC BRAIN INJURY Research Overview
Co-Morbidities Associated with mTBI and PTSD
Chronic Pain N=277 81.5%
PTSD N=232 68.2%
TBI N=227 66.8%
16.5%
2.9%
10.3%
42.1%
12.8%
6.8%
5.3%
•Sleep disorders
•Substance abuse
•Psychiatric illness
•Vestibular disorders
•Visual disorders
•Cognitive disorders
Lew, et al: "Prevalence of Chronic Pain, Posttraumatic Stress Disorder, and Persistent Postconcussive Symptoms in OIF/OEF Veterans: Polytrauma Clinical Triad", Dept. of Veterans Affairs, Journal of Rehabilitative Research and Development, Vol. 46, No. 6, 2009, pp. 697-702, Fig. 1
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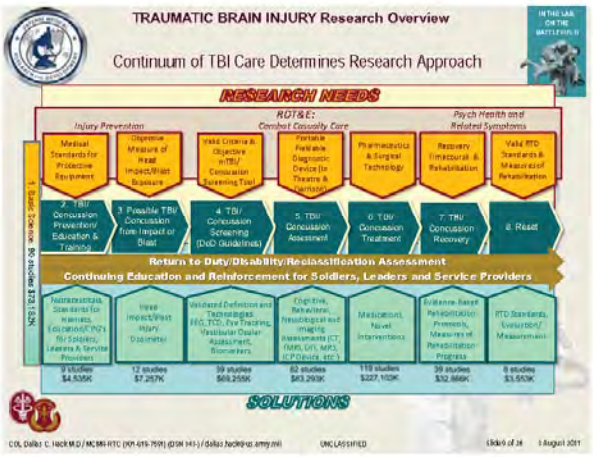
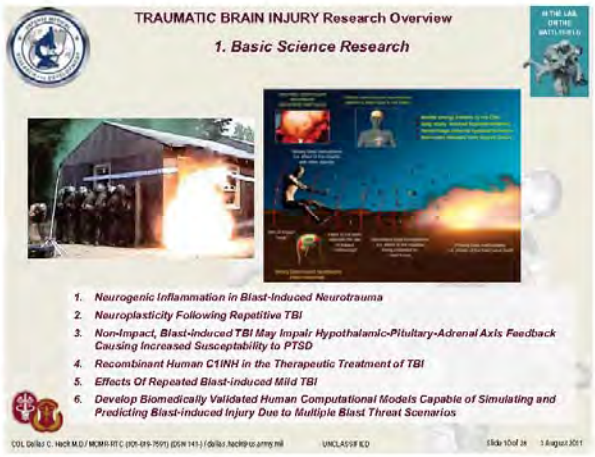
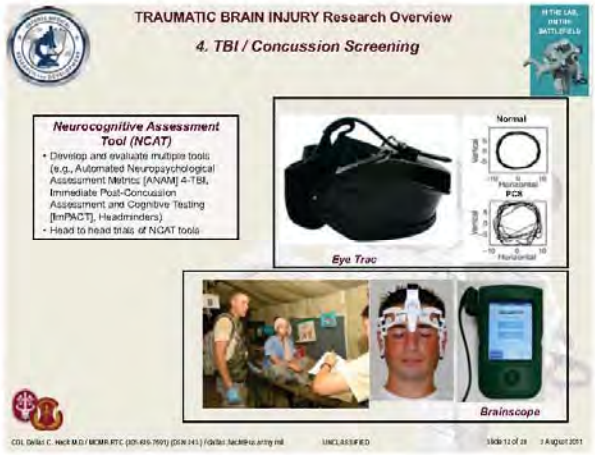
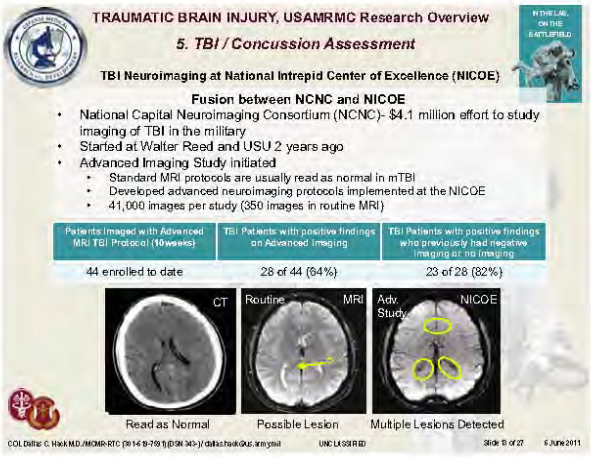

TRAUMATIC BRAIN INJURY Research Overview
Continuum of TBI Care Determines Research Approach
RESEARCH NEEDS
Injury Prevention
RDT&E
Combat Casualty Care
Psych Health and Related Symptoms
Return to Duty/Disability/Reclassification Assessment
Continuing Education and Reinforcement for Soldiers, Leaders and Service Providers
SOLUTIONS

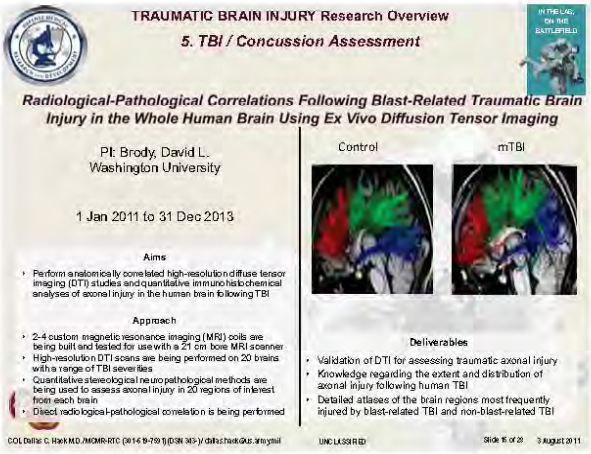

TRAUMATIC BRAIN INJURY Research Overview
1. Basic Science Research
1. Neurogenic Inflammation in Blast-Induced Neurotrauma
2. Neuroplasticity Following Repetitive TBI
3. Non-Impact, Blast-induced TBI May Impair Hypothalamic-Pituitary-Adrenal Axis Feedback Causing Increased Susceptability to PTSD
4. Recombinant Human C1INH in the Therapeutic Treatment of TBI
5. Effects Of Repeated Blast-induced Mild TBI
6. Develop Biomedically Validated Human Computational Models Capable of Simulating and Predicting Blast-induced Injury Due to Multiple Blast Threat Scenarios

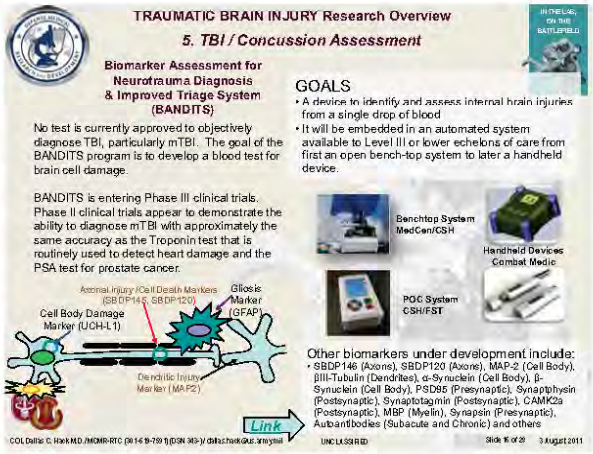

TRAUMATIC BRAIN INJURY Research Overview
2. TBI / Concussion Prevention and Protection
1. High Dose Omega-3 (n-3) Fatty Acid Supplementation in Traumatic Brain Injury
2. DHA for Neuroprotection and Resilience
3. Possible TBI/ Concussion from Impact or Blast
1. Helmet Mounted Sensor System (HMSS) – "Gen II"
SMAKR
HEADS
Helmet Mounted Sensor System Improved Capabilities:
• Wireless downloading
• 6-axis accelerometers
• 12-month battery life
2. DARPA Blast Gauge
Status LEDs
Status button
Pressure dome
USB
Designed to quantify blast pressure exposure:
• Assist triage (status lights)
• Provide data (USB download)
• Rapid development (11 months)
• Flexibility (Mounting, Reprogrammable, Disposable)

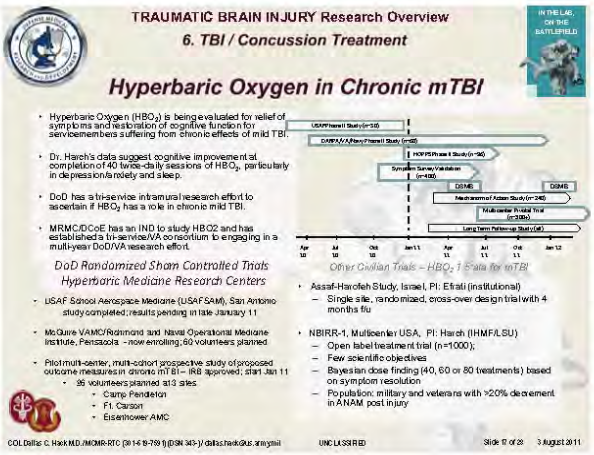

TRAUMATIC BRAIN INJURY Research Overview
4. TBI / Concussion Screening
Neurocognitive Assessment Tool (NCAT)
• Develop and evaluate multiple tools (e.g., Automated Neuropsychological Assessment Metrics [ANAM] 4-TBI, Immediate Post-Concussion Assessment and Cognitive Testing [ImPACT], Headminders)
• Head to head trials of NCAT tools
Normal
PCS
Eye Trac
Brainscope


TRAUMATIC BRAIN INJURY, USAMRMC Research Overview
5. TBI / Concussion Assessment
TBI Neuroimaging at National Intrepid Center of Excellence (NICOE)
Fusion between NCNC and NICOE
National Capital Neuroimaging Consortium (NCNC)- $4.1 million effort to study imaging of TBI in the military
Started at Walter Reed and USU 2 years ago
Advanced Imaging Study initiated
Standard MRI protocols are usually read as normal in mTBI
Developed advanced neuroimaging protocols implemented at the NICOE
41,000 images per study (350 images in routine MRI)
Patients Imaged with Advanced MRI TBI Protocol (10weeks)
TBI Patients with positive findings on Advanced Imaging
TBI Patients with positive findings who previously had negative imaging or no imaging
44 enrolled to date
28 of 44 (64%)
23 of 28 (82%)
CT
Routine MRI
Adv. Study NICOE
Read as Normal
Possible Lesion
Multiple Lesions Detected


TRAUMATIC BRAIN INJURY Research Overview
PT075299
Advanced MRI in Blast-Related TBI
Brody, David L.
Washington University
1 Sep 2008 to 30 Jul 2011
The NEW ENGLAND JOURNAL of MEDICINE
Detection of Blast-Related Traumatic Brain Injury in U.S. Military Personnel
Aims
Assess the extent of acute blast TBI-related abnormalities using diffusion tensor imaging (DTI) and resting-state functional magnetic resonance imaging (fMRI)
Develop acute imaging predictors of overall 6- to 12-month TBI-related clinical outcomes
Approach
Initial DTI, resting-state fMRI, and MRI scans are being acquired on blast-related TBI patients at Landstuhl Regional Medical Center within 4 days of injury
Participants detailed clinical data, including neuropsychological, cognitive, and motor tests, and repeat imaging scans are collected 6-12 months after injury
Analyses are being performed to develop optimal acute imaging predictors of global outcome and specific post-traumatic deficits
Deliverables
Evaluation of the extent of abnormalities and acute axonal injury that result from blast-related TBI using DTI and resting-state fMRI
Identification of a set of clinical relevant acute imaging predictors of post-traumatic deficits and disorders, including motor and learning deficits, depression, and post-traumatic stress disorder
Status
Funded and open
A 9-month extension with an additional $200,000 from RAD2 was granted
Initial results published in 2 June NEJM


TRAUMATIC BRAIN INJURY Research Overview
5. TBI / Concussion Assessment
Radiological-Pathological Correlations Following Blast-Related Traumatic Brain Injury in the Whole Human Brain Using Ex Vivo Diffusion Tensor Imaging
PI: Brody, David L.
Washington University
1 Jan 2011 to 31 Dec 2013
Aims
Perform anatomically correlated high-resolution diffuse tensor imaging (DTI) studies and quantitative immunohistochemical analyses of axonal injury in the human brain following TBI
Approach
2-4 custom magnetic resonance imaging (MRI) coils are being built and tested for use with a 21 cm bore MRI scanner
High-resolution DTI scans are being performed on 20 brains with a range of TBI severities
Quantitative stereological neuropathological methods are being used to assess axonal injury in 20 regions of interest from each brain
Direct radiological-pathological correlation is being performed
Control
mTBI
Deliverables
Validation of DTI for assessing traumatic axonal injury
Knowledge regarding the extent and distribution of axonal injury following human TBI
Detailed atlases of the brain regions most frequently injured by blast-related TBI and non-blast-related TBI


TRAUMATIC BRAIN INJURY Research Overview
5. TBI / Concussion Assessment
Biomarker Assessment for Neurotrauma Diagnosis & Improved Triage System (BANDITS)
No test is currently approved to objectively diagnose TBI, particularly mTBI. The goal of the BANDITS program is to develop a blood test for brain cell damage.
BANDITS is entering Phase III clinical trials. Phase II clinical trials appear to demonstrate the ability to diagnose mTBI with approximately the same accuracy as the Troponin test that is routinely used to detect heart damage and the PSA test for prostate cancer.
Axonal Injury / Cell Death Markers (SBDP145, SBDP120)
Gliosis Marker (GFAP)
Cell Body Damage Marker (UCH-L1)
Dendritic Injury Marker (MAP2)
Link
GOALS
A device to identify and assess internal brain injuries from a single drop of blood
It will be embedded in an automated system available to Level III or lower echelons of care from first an open bench-top system to later a handheld device.
Benchtop System MedCen/CSH
Handheld Devices Combat Medic
POC System CSH/FST
Other biomarkers under development include:
SBDP146 (Axons), SBDP120 (Axons), MAP-2 (Cell Body), βIII-Tubulin (Dendrites), α-Synuclein (Cell Body), β-Synuclein (Cell Body), PSD95 (Presynaptic), Synaptophysin (Postsynaptic), Synaptotagmin (Postsynaptic), CAMK2a (Postsynaptic), MBP (Myelin), Synapsin (Presynaptic), Autoantibodies (Subacute and Chronic) and others


TRAUMATIC BRAIN INJURY Research Overview
6. TBI / Concussion Treatment
Hyperbaric Oxygen in Chronic mTBI
DoD Randomized Sham Controlled Trials
Hyperbaric Medicine Research Centers
Other Civilian Trials – HBO2 Data for mTBI
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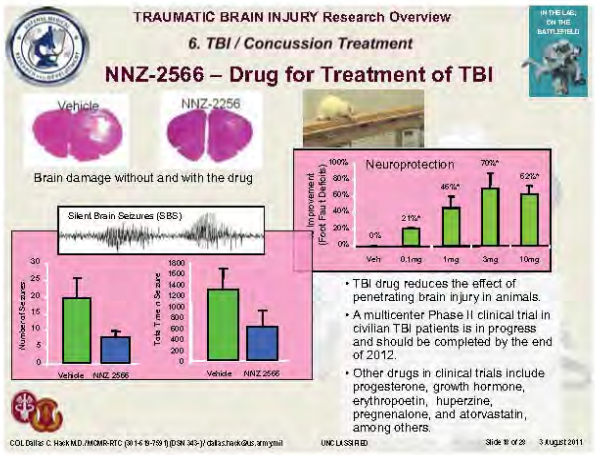
TRAUMATIC BRAIN INJURY Research Overview
6. TBI / Concussion Treatment
NNZ-2566 – Drug for Treatment of TBI
Vehicle
NNZ-2256
Brain damage without and with the drug
Silent Brain Seizures (SBS)
Neuroprotection
• TBI drug reduces the effect of penetrating brain injury in animals.
• A multicenter Phase II clinical trial in civilian TBI patients is in progress and should be completed by the end of 2012.
• Other drugs in clinical trials include progesterone, growth hormone, erythropoetin, huperzine, pregnenalone, and atorvastatin, among others.
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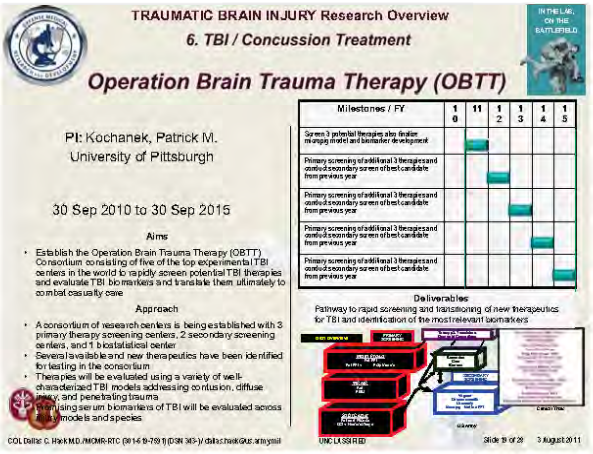
TRAUMATIC BRAIN INJURY Research Overview
6. TBI / Concussion Treatment
Operation Brain Trauma Therapy (OBTT)
PI: Kochanek, Patrick M.
University of Pittsburgh
30 Sep 2010 to 30 Sep 2015
Aims
Approach
Deliverables
UNCLASSIFIED


TRAUMATIC BRAIN INJURY Research Overview
6. TBI / Concussion Treatment
Combination Therapies for Penetrating Brain Injury: An Experimental Approach
PI: Lu, May
Walter Reed Army Institute of Research
1 Feb 2010 to 30 Sep 2012
Aims
Approach
Deliverables
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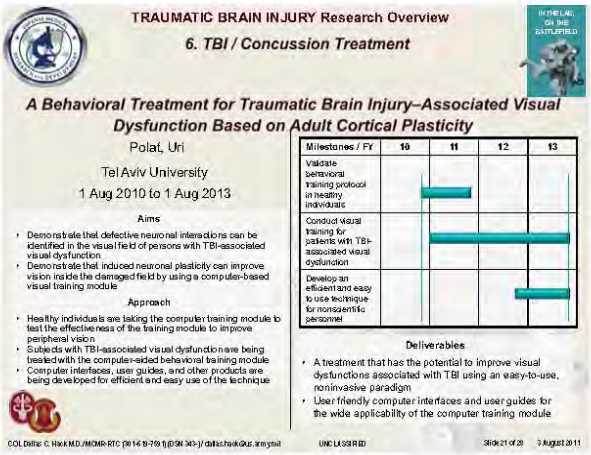
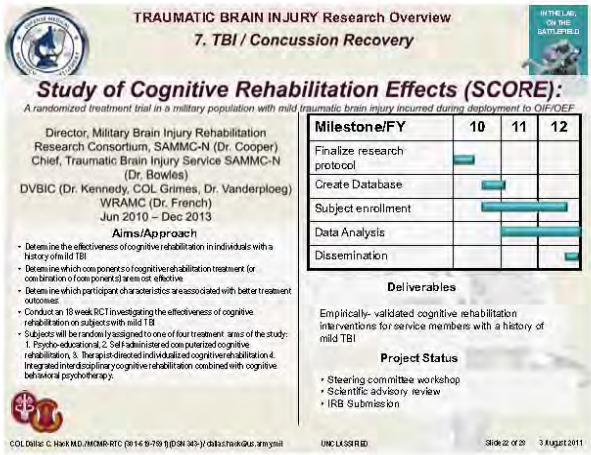
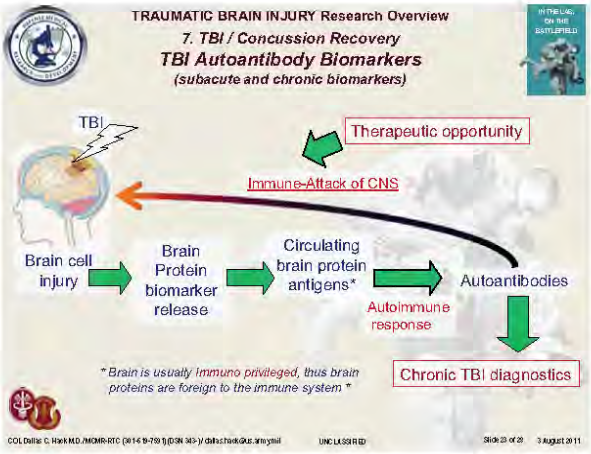
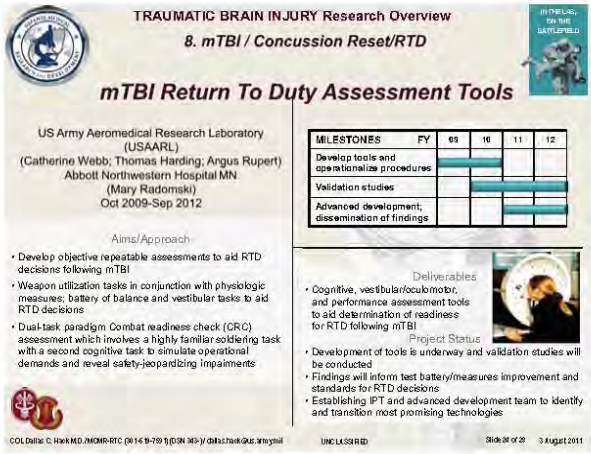

TRAUMATIC BRAIN INJURY Research Overview
6. TBI / Concussion Treatment
A Behavioral Treatment for Traumatic Brain Injury–Associated Visual Dysfunction Based on Adult Cortical Plasticity
Polat, Uri
Tel Aviv University
1 Aug 2010 to 1 Aug 2013
Aims
Demonstrate that defective neuronal interactions can be identified in the visual field of persons with TBI-associated visual dysfunction
Demonstrate that induced neuronal plasticity can improve vision inside the damaged field by using a computer-based visual training module
Approach
Healthy individuals are taking the computer training module to test the effectiveness of the training module to improve peripheral vision
Subjects with TBI-associated visual dysfunction are being treated with the computer-aided behavioral training module
Computer interfaces, user guides, and other products are being developed for efficient and easy use of the technique
Milestones / FY 10 11 12 13
Validate behavioral training protocol in healthy individuals
Conduct visual training for patients with TBI-associated visual dysfunction
Develop an efficient and easy to use technique for nonscientific personnel
Deliverables
A treatment that has the potential to improve visual dysfunctions associated with TBI using an easy-to-use, noninvasive paradigm
User friendly computer interfaces and user guides for the wide applicability of the computer training module
UNCLASSIFIED
3 August 2011


TRAUMATIC BRAIN INJURY Research Overview
7. TBI / Concussion Recovery
Study of Cognitive Rehabilitation Effects (SCORE):
A randomized treatment trial in a military population with mild traumatic brain injury incurred during deployment to OIF/OEF
Director, Military Brain Injury Rehabilitation Research Consortium, SAMMC-N (Dr. Cooper)
Chief, Traumatic Brain Injury Service SAMMC-N (Dr. Bowles)
DVBIC (Dr. Kennedy, COL Grimes, Dr. Vanderploeg)
WRAMC (Dr. French)
Jun 2010 – Dec 2013
Aims/Approach
Determine the effectiveness of cognitive rehabilitation in individuals with a history of mild TBI
Determine which components of cognitive rehabilitation treatment (or combination of components) are most effective
Determine which participant characteristics are associated with better treatment outcomes
Conduct an 18 week RCT investigating the effectiveness of cognitive rehabilitation on subjects with mild TBI
Subjects will be randomly assigned to one of four treatment arms of the study: 1. Psycho-educational, 2. Self-administered computerized cognitive rehabilitation, 3. Therapist-directed individualized cognitive rehabilitation 4. Integrated interdisciplinary cognitive rehabilitation combined with cognitive behavioral psychotherapy.
Milestone/FY 10 11 12
Finalize research protocol
Create Database
Subject enrollment
Data Analysis
Dissemination
Deliverables
Empirically- validated cognitive rehabilitation interventions for service members with a history of mild TBI
Project Status
Steering committee workshop
Scientific advisory review
IRB Submission
UNCLASSIFIED
3 August 2011


TRAUMATIC BRAIN INJURY Research Overview
7. TBI / Concussion Recovery
TBI Autoantibody Biomarkers
(subacute and chronic biomarkers)
TBI
Therapeutic opportunity
Immune-Attack of CNS
Brain cell injury
Brain Protein biomarker release
Circulating brain protein antigens*
Autoantibodies
Autoimmune response
Chronic TBI diagnostics
* Brain is usually immuno privileged, thus brain proteins are foreign to the immune system *
UNCLASSIFIED
3 August 2011


TRAUMATIC BRAIN INJURY Research Overview
8. mTBI / Concussion Reset/RTD
mTBI Return To Duty Assessment Tools
US Army Aeromedical Research Laboratory (USAARL)
(Catherine Webb; Thomas Harding; Argus Rupert)
Abbott Northwestern Hospital MN
(Mary Radomski)
Oct 2009-Sep 2012
Aims/Approach
Develop objective repeatable assessments to aid RTD decisions following mTBI
Weapon utilization tasks in conjunction with physiologic measures; battery of balance and vestibular tasks to aid RTD decisions
Dual-task paradigm Combat readiness check (CRC) assessment which involves a highly familiar soldiering task with a second cognitive task to simulate operational demands and reveal safety-jeopardizing impairments
MILESTONES FY 09 10 11 12
Develop tools and operationalize procedures
Validation studies
Advanced development; dissemination of findings
Deliverables
Cognitive, vestibular/oculomotor, and performance assessment tools to aid determination of readiness for RTD following mTBI
Project Status
Development of tools is underway and validation studies will be conducted
Findings will inform test battery/measures improvement and standards for RTD decisions
Establishing IPT and advanced development team to identify and transition most promising technologies
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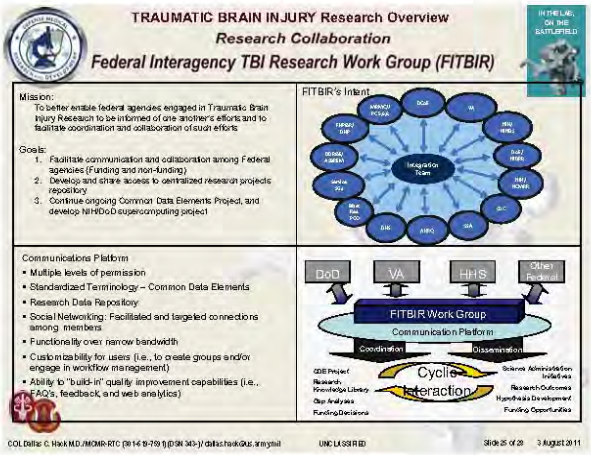
3 August 2011


TRAUMATIC BRAIN INJURY Research Overview
Research Collaboration
Federal Interagency TBI Research Work Group (FITBIR)
Mission:
To better enable federal agencies engaged in Traumatic Brain Injury Research to be informed of one another's efforts and to facilitate coordination and collaboration of such efforts
Goals:
1. Facilitate communication and collaboration among Federal agencies (Funding and non-funding)
2. Develop and share access to centralized research projects repository
3. Continue ongoing Common Data Elements Project, and develop NIH/DoD supercomputing project
FITBIR's Intent
Integration Team
Communications Platform
• Multiple levels of permission
• Standardized Terminology – Common Data Elements
• Research Data Repository
• Social Networking: Facilitated and targeted connections among members
• Functionality over narrow bandwidth
• Customizability for users (i.e., to create groups and/or engage in workflow management)
• Ability to "build-in" quality improvement capabilities (i.e., FAQ's, feedback, and web analytics)
DoD
VA
HHS
Other Federal
FITBIR Work Group
Communication Platform
Coordination
Dissemination
Cyclic Interaction
CDE Project
Research Knowledge Library
Data Analyses
Funding Decisions
Science Administration Initiatives
Research Outcomes
Hypothesis Development
Funding Opportunities
IN THE LAB, ON THE BATTLEFIELD
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TRAUMATIC BRAIN INJURY Research Overview
Research Collaboration, cont.
Common Data Elements
• Quad Agency Initiative: NIH, DoD, VA, CDC
• Global Aim: Develop Common language/ terminology and refine standards for data collection to rapidly advance research by combining comparable large TBI patient populations.
• Imaging MRI/CT: Adopt Technical Standards/Secure Internet Transfer of Images
• Establish Core Demographics and Outcome measures
• Biomarkers: Establish SOP for Processing, Storage and Shipping. Core elements- DNA, proteomics, endocrine,
• DoD and Civilian partnership to develop national database with Academic, federal DoD steering committee.
• http://www.commondataelements.ninds.nih.gov/
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TRAUMATIC BRAIN INJURY Research Overview
Research Consortium
Traumatic Brain Injury Multidisciplinary Research Consortium
Award Details
• "Mission Connect"
• Co-directors – Drs. John Holcomb (University of Texas Health Science Center [UTHSC]) and Claudia Robertson (Baylor College of Medicine (BCM))
• Twenty awards made to four academic institutions (UTHSC, BCM, University of Texas Medical Branch and Rice University)
• Award date August 1, 2008
• Five year period of performance (2008-2013)
• Combined budget of $36M
• Progress tracked by review of quarterly and annual progress reports from each PI
Research Focus
Vision: to improve the diagnosis and treatment of mTBI through collaborative basic and clinical research
• Diagnosis of mTBI: Observational and intervention clinical trial to improve the diagnosis of mTBI [one integrated clinical protocol across several institutions and collaborating PIs]
• Characterize rat models: investigating five models of mTBI including fluid percussion, cortical impact and blast, with and without polytrauma
• Develop new and innovative treatment strategies for mTBI: [5 projects on neuroprotection and 6 projects on regeneration]
External Advisory Board
• Members drawn from federal agencies (Defense Center of Excellence, OTSG, NIH, VA, USAMRMC, DoD/VA Vision Center of Excellence), academic institutions and one retired military TBI survivor
• Provide independent expertise and advice to the Grant Officers Representative (GOR) to facilitate consortium progress based on review of progress reports
Research Progress
• Completed second year of awards
• Progress reviewed quarterly by EAB and GOR
• Excellent progress on individual non-clinical projects
• Rat model of mTBI plus hemorrhage for 60 minutes confirmed to result in a more severe outcome; erythropoietin (Epo), and derivatives are being studied in this model with promising results for Epo derivative ARA290
• Recruitment is a significant limiting factor for the clinical projects and is the topic of ongoing discussions with the consortium leadership
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TRAUMATIC BRAIN INJURY Research Overview
Research Center
USUHS Center for Neuroscience and Regenerative Medicine
Neuropathology: Major Goals
• Determine pathological features of mild TBI
• Comparative analysis to repetitive sports injuries to evaluate tau and CTE.
• Comparative analysis across the spectrum of TBI experienced in military (deliberating, closed head, blast, blast plus, repetitive exposures, w/ anxiety)
• Focus analyses on mechanisms of damage/degeneration that can inform future therapeutic interventions-Examine acute and chronic injuries to evaluate long term consequences
• Biologic markers–correlate expression with damage sites and features
• Neuroimaging/signals–translate pathological features to patient imaging
• Phenotyping data–connect brain pathology with functional deficits, validate clinical and diagnostic criteria to advance all studies in TBI field
• Outcomes–correlate operational exposures to clinical outcomes (including behavioral/psychiatric manifestations)
• 20 year old Ivy League football player.
• Reported having difficulty "coping with school", committed suicide.
• Tau stains demonstrating focal perivascular lesions in frontal and insular cortex. Diagnosis – early CTE
Neuropathology: NFL and CTE
• In order to study the brain pathology which occurs following a career in professional football Dr. Peil has examined a series of brain specimens derived from former NFL football players, age matched controls and former professional boxers.
• Data obtained to date indicates that the retired NFL players develop a form of slowly progressive neurodegenerative disease called chronic traumatic encephalopathy, a neuropathologically distinct disorder that prior to these studies had almost exclusively been described in former boxers. The changes in the brains of the former football players are virtually identical to those seen in the boxers.
• We expect this collaboration to continue and to expand in order to make comparisons between the football players and what is seen following mTBI in soldiers.
CTE in a 45 year old former NFL linebacker.
• Beginning at age 55, he developed apathy, dysarthria, inattention, outbursts of anger and short term memory problems.
• Tau stain demonstrating prominent involvement of amygdala, hippocampus, temporal and insular cortex.
• CTE in 45 year old former NFL linebacker.
• At age 42: short term memory loss, depression, inattention, poor executive function noted. Became addicted to cocaine (died of an overdose).
• Tau stain showing prominent involvement of amygdala(a), temporal cortex (t) and hippocampus.
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TRAUMATIC BRAIN INJURY Research Overview

Backup Slides

TRAUMATIC BRAIN INJURY Research Overview

Why Biomarkers Matter?

- Useful in the elucidation of pathogenesis, in improving early diagnosis, in predicting outcome, and in the identification and evaluation of targets for the implementation and evaluation of therapeutic agents.
- Ideal biomarker in TBI would have some or many of the following characteristics:
  - provided the ability to track individual response
  - be absent under normal conditions
  - be present rapidly post-injury
  - be easily accessible and measurable in biofluids
  - have an absolute value proportional to the extent of damage
  - allow for the establishment of a link with pathophysiologic processes

TRAUMATIC BRAIN INJURY Research Overview

BANDITS PROGRAM
Clinical Trials Towards FDA Approval

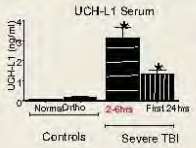
- Pilot study = first in human experience to determine if it is possible to detect markers
- Feasibility study = explore the biomarker validity in applicable patient population and generate data to establish diagnostic claims
- Pivotal study = satisfy clinical regulatory requirements needed to support premarket authorization by FDA by production of results to confirm the diagnostic claims

CURRENT AND PLANNED CLINICAL TRIALS

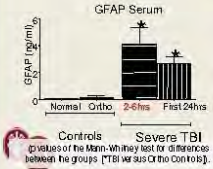
TYPE OF STUDY	TBI SEVERITY	# OF PATIENTS	STATUS
Feasibility Study	Severe TBI	200	200 Patients enrolled
Pilot Study	Mild-Moderate TBI	50	• Complete • Data analysis in progress
Feasibility Study	Mild-Moderate TBI	350	201 Enrolled
Reference Range Study	Non Acute TBI	Phase I 750 Phase II 1500	Phase I 750 Enrolled
Pivotal Study	Mild-Moderate-Severe TBI	1200	• Will use an automated benchtop device and POC • June 2011 initiated according to schedule, enrollment completion Q4'12

TRAUMATIC BRAIN INJURY Research Overview

BANDITS PROGRAM
Biomarkers in Severe TBI Patients

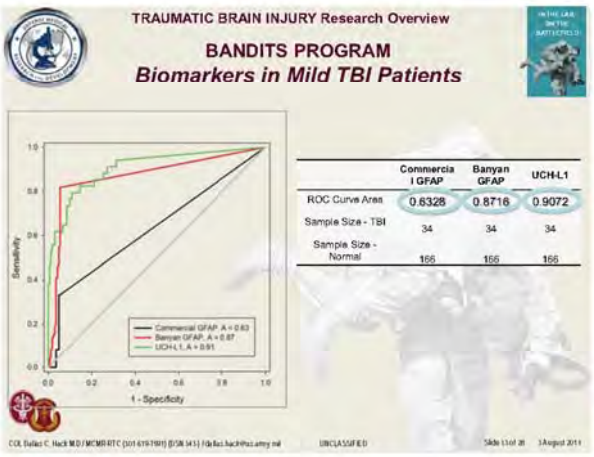


UCH-L1 (Serum)	#	Mean	SEM	P value
Normal	176	0.06	0.004	
Ortho	11	0.16	1.04	
TBI 2-6 hrs	37	3.140	0.53	*<0.0001
TBI 24 hrs	101	1.35	0.18	* 0.0005



GFAP (Serum)	#	Mean	SEM	P value
Normal	176	0.06	0.008	
Ortho	11	0.13	0.13	
TBI 2-6 hrs	37	4.08	1.22	*<0.0001
TBI 24 hrs	101	2.65	0.49	*<0.0001

p values of the Mann-Whitney test for differences between the groups (*TBI versus Ortho Controls).


TRAUMATIC BRAIN INJURY Research Overview
BANDITS PROGRAM
Biomarkers in Mild TBI Patients
Sensitivity
1 - Specificity
Commercial GFAP A = 0.83
Banyan GFAP A = 0.87
UCH-L1 A = 0.91
Commercial GFAP
Banyan GFAP
UCH-L1
ROC Curve Area
0.8328
0.8716
0.9072
Sample Size - TBI
34
34
34
Sample Size - Normal
166
166
166
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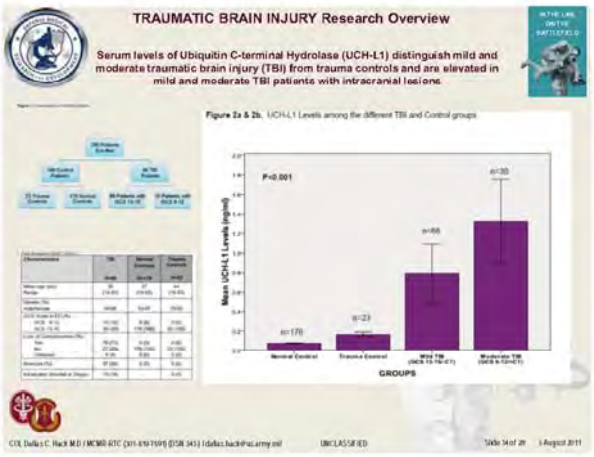
TRAUMATIC BRAIN INJURY Research Overview
Serum levels of Ubiquitin C-terminal Hydrolase (UCH-L1) distinguish mild and moderate traumatic brain injury (TBI) from trauma controls and are elevated in mild and moderate TBI patients with intracranial lesions
Figure 2a & 2b. UCH-L1 Levels among the different TBI and Control groups
P<0.001
n=178
n=23
n=66
n=30
Mean UCH-L1 Levels (ng/ml)
GROUPS
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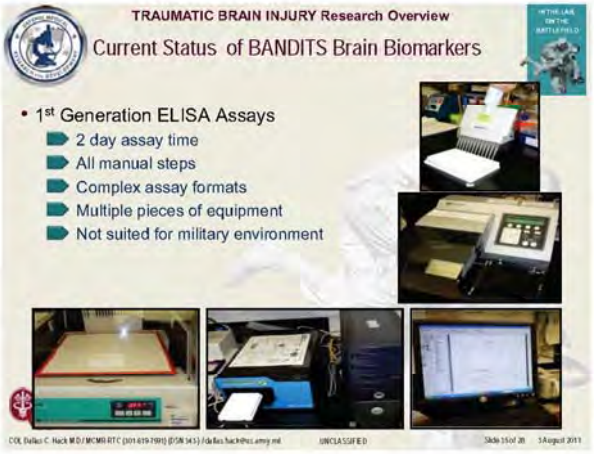
TRAUMATIC BRAIN INJURY Research Overview
Current Status of BANDITS Brain Biomarkers
• 1st Generation ELISA Assays
2 day assay time
All manual steps
Complex assay formats
Multiple pieces of equipment
Not suited for military environment
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TRAUMATIC BRAIN INJURY Research Overview
Current Status of BANDITS Brain Biomarkers
• 2nd Generation ELISA Assays
4 hr assay time
manual steps with semi automation
Complex assay formats
Single to dual piece of equipment
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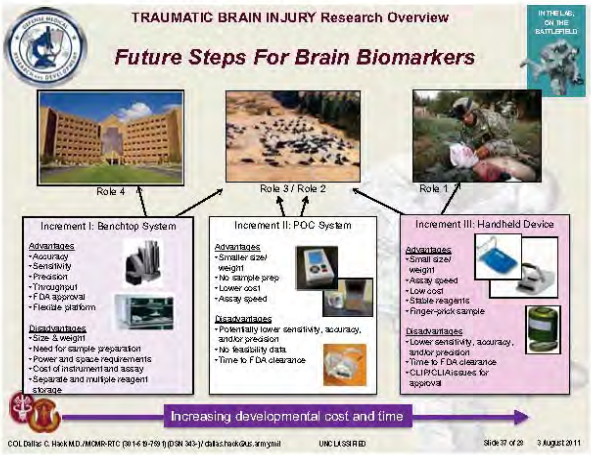
TRAUMATIC BRAIN INJURY Research Overview
Future Steps For Brain Biomarkers
Role 4
Role 3 / Role 2
Role 1
Increment I: Benchtop System
Advantages
•Accuracy
•Sensitivity
•Precision
•Throughput
•FDA approval
•Flexible platform
Disadvantages
•Size & weight
•Need for sample preparation
•Power and space requirements
•Cost of instrument and assay
•Separate and multiple reagent storage
Increment II: POC System
Advantages
•Smaller size/ weight
•No sample prep
•Lower cost
•Assay speed
Disadvantages
•Potentially lower sensitivity, accuracy, and/or precision
•No feasibility data
•Time to FDA clearance
Increment III: Handheld Device
Advantages
•Small size/ weight
•Assay speed
•Low cost
•Stable reagents
•Finger-prick sample
Disadvantages
•Lower sensitivity, accuracy, and/or precision
•Time to FDA clearance
•CLIA/CLIA issues for approval
Increasing developmental cost and time
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TRAUMATIC BRAIN INJURY Research Overview
Clinical Update
• Clinical Studies Update
– Severe TBI Study - complete
– MMTBI Study on schedule
– Normal Population Study – first phase complete
– Clinical Samples Stability - ongoing
– Pivotal Study – initiated / on schedule
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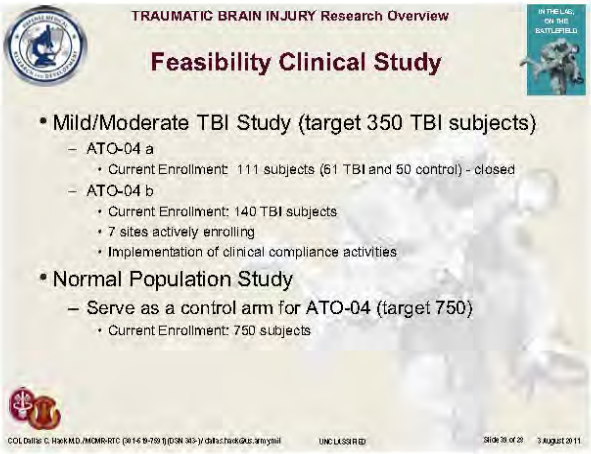
TRAUMATIC BRAIN INJURY Research Overview
Feasibility Clinical Study
• Mild/Moderate TBI Study (target 350 TBI subjects)
– ATO-04 a
• Current Enrollment: 111 subjects (61 TBI and 50 control) - closed
– ATO-04 b
• Current Enrollment: 140 TBI subjects
• 7 sites actively enrolling
• Implementation of clinical compliance activities
• Normal Population Study
– Serve as a control arm for ATO-04 (target 750)
• Current Enrollment: 750 subjects
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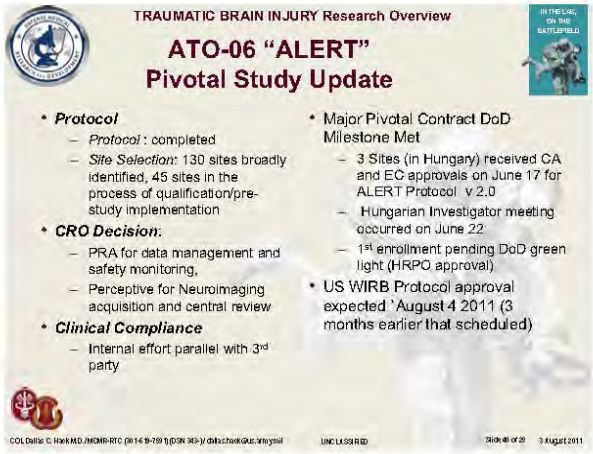
TRAUMATIC BRAIN INJURY Research Overview
ATO-06 "ALERT"
Pivotal Study Update
• Protocol
– Protocol : completed
– Site Selection: 130 sites broadly identified, 45 sites in the process of qualification/pre-study implementation
• CRO Decision:
– PRA for data management and safety monitoring,
– Perceptive for Neuroimaging acquisition and central review
• Clinical Compliance
– Internal effort parallel with 3rd party
• Major Pivotal Contract DoD Milestone Met
– 3 Sites (in Hungary) received CA and EC approvals on June 17 for ALERT Protocol v 2.0
– Hungarian Investigator meeting occurred on June 22
– 1st enrollment pending DoD green light (HRPO approval)
• US WIRB Protocol approval expected ' August 4 2011 (3 months earlier that scheduled)
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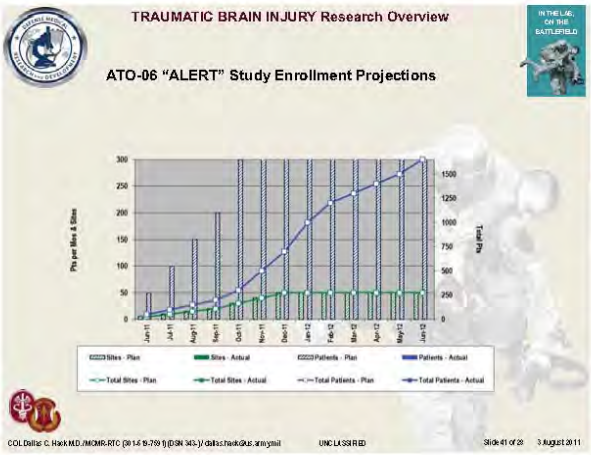
TRAUMATIC BRAIN INJURY Research Overview
ATO-06 "ALERT" Study Enrollment Projections
Sites - Plan
Sites - Actual
Patients - Plan
Patients - Actual
Total Sites - Plan
Total Sites - Actual
Total Patients - Plan
Total Patients - Actual
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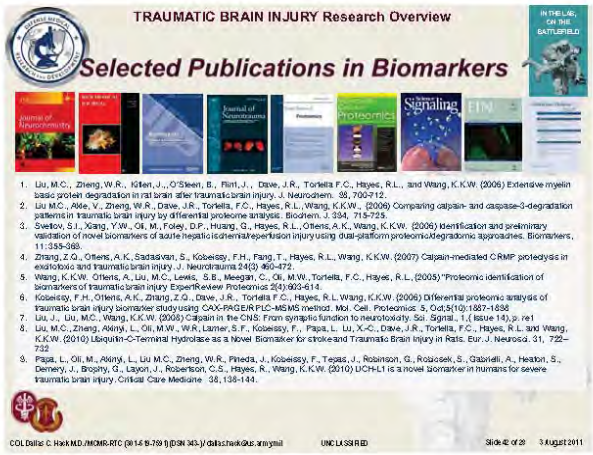
TRAUMATIC BRAIN INJURY Research Overview
Selected Publications in Biomarkers
1. Liu, M.C., Zheng, W.R., Kilen, J.., O'Steen, B., Flint, J., Dave, J.R., Tortella F.C., Hayes, R.L., and Wang, K.K.W. (2006) Extensive myelin basic protein degradation in rat brain after traumatic brain injury. J. Neurochem. 98, 700-712.
2. Liu M.C., Akle, V., Zheng, W.R., Dave, J.R., Tortella, F.C., Hayes, R.L., Wang, K.K.W., (2006) Comparing calpain- and caspase-3-degradation patterns in traumatic brain injury by differential proteome analysis. Biochem. J. 394, 715-725.
3. Svetlov, S.I., Xiang, Y.W., Oli, M., Foley, D.P., Huang, Q., Hayes, R.L., Ottens, A.K., Wang, K.K.W. (2006) Identification and preliminary validation of novel biomarkers of acute hepatic ischemia/reperfusion injury using dual-platform proteomic/degradomic approaches. Biomarkers, 11:355-369.
4. Zhang, Z.Q., Ottens, A.K., Sadasivan, S., Kobeissy, F.H., Fang, T., Hayes, R.L., Wang, K.K.W. (2007) Calpain-mediated CRMP proteolysis in excitotoxic and traumatic brain injury. J. Neurotrauma 24(3) 460-472.
5. Wang, K.K.W. Ottens, A., Liu, M.C., Lewis, S.B., Meegan, C., Oli, M.W., Tortella, F.C., Hayes, R.L. (2005) "Proteomic identification of biomarkers of traumatic brain injury ExpertReview Proteomics 2(4):603-614.
6. Kobeissy, F.H., Ottens, A.K., Zhang, Z.Q., Dave, J.R., Tortella F.C., Hayes, R.L. Wang, K.K.W. (2006) Differential proteomic analysis of traumatic brain injury biomarker study using CAX-PAGE/RPLC-MSMS method. Mol. Cell. Proteomics: 5, Oct;5(10):1887-1898
7. Liu, J., Liu, M.C., Wang, K.K.W. (2008) Calpain in the CNS: From synaptic function to neurotoxicity. Sci. Signal., 1,(Issue 14), p. re1
8. Liu, M.C., Zheng, Akinyi, L., Oli, M.W., W.R, Lamer, S.F., Kobeissy, F., Papa, L. Lu, X-C., Dave, J.R., Tortella, F.C., Hayes, R.L. and Wang, K.K.W. (2010) Ubiquitin-C-Terminal Hydrolase as a Novel Biomarker for stroke and Traumatic Brain Injury in Rats. Eur. J. Neurosci. 31, 722–732
9. Papa, L., Oli, M., Akinyi, L., Liu M.C., Zheng, W.R., Pineda, J., Kobeissy, F., Texas, J., Robinson, G., Robicsek, S., Gabrielli, A., Heaton, S., Demery, J., Brophy, G., Layon, J., Robertson, C.S., Hayes, R., Wang, K.K.W. (2010) UCH-L1 is a novel biomarker in humans for severe traumatic brain injury. Critical Care Medicine 38, 138-144.
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TRAUMATIC BRAIN INJURY Research Overview
Additional Publications
10. Brophy G, Pineda J, Papa L, et al. αII-Spectrin Breakdown Product Cerebrospinal Fluid Exposure Metrics Suggest Differences in Cellular Injury Mechanisms after Severe Traumatic Brain Injury J Neurotrauma. 2009 April; 26(4): 471–479.
11. Brophy G, Mondello S, Papa L, et al. Biokinetic Analysis of Ubiquitin C-Terminal Hydrolase-L1 (UCH-L1) in Severe Traumatic Brain Injury Patient Biofluids J Neurotrauma. 2011 Apr 8.
12. Liu M, Akinyi L, Scharf D, Ubiquitin C-terminal hydrolase-L1 as a biomarker for ischemic and traumatic brain injury in rats Eur J Neurosci. 2010 Feb; 31(4):722-32.
13. Mondello S, Robicsek S, Gabrielli A, et al. αII-spectrin breakdown products (SBDPs): diagnosis and outcome in severe traumatic brain injury patients J Neurotrauma. 2010 Jul;27 (7):1203-13.
14. Mondello S, Muller U, Jeromin A, et al. Blood-based diagnostics of traumatic brain injuries Expert Rev Mol Diagn. 2011 Jan;11(1):65-78.
15. Papa L, Akinyi L, Liu M, et al. Ubiquitin C-terminal hydrolase is a novel biomarker in humans for severe traumatic brain injury Crit Care Med. 2010 Jan;38(1):138-44.
16. Papa L, Robinson G, Oli M, et al. Use of biomarkers for diagnosis and management of traumatic brain injury patients Expert Opinion on Medical Diagnostics Aug 2008, Vol. 2, No. 8, Pages 937-945. 937-945.
17. Papa et al. Serum levels of Ubiquitin C-terminal Hydrolase (UCH-L1) distinguish mild and moderate traumatic brain injury (TBI) from trauma controls and are elevated in mild and moderate TBI patients with intracranial lesions. In print J Trauma 2011
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TRAUMATIC BRAIN INJURY Research Overview
Other Brain Injury Biomarkers
Biomarker
Anatomical Location
ELISA Sensitive in CSF
ELISA Sensitive in Serum
Proof-of-Concept
Validation
SBDP145 Axons
SBDP120 Axons
UCH-L1 Cell Body
MAP-2 Dendrites
βIII-Tubulin Dendrites
α-Synuclein Cell Body
β-Synuclein Cell Body
PSD95 Postsynaptic
Synaptophysin Presynaptic
Synaptotagmin Postsynaptic
CAMK2a Postsynaptic
MBP Myelin
Synapsin Presynaptic
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TRAUMATIC BRAIN INJURY Research Overview

Other TBI Biomarker Exemplar Projects

Sep 10 – Sep 13	Ahlers, Stephen/ NMRC	Neurocognitive and Biomarker Evaluation of Combination mTBI from Blast Overpressure and Traumatic Stress
Apr 09 –	Ahlers, Stephen/ NMRC	Neuroimaging of Biomarkers for Combat Relevant Traumatic Brain Injury
Feb 10 – Jun 13	Calvin Goforth/ SRC Fluidics	Microassay Diagnostic Device for Rapid Assessment of Traumatic Brain Injury
Aug 05 – Jul 06	Clarke, Jean/ Nomadics, Inc.	Multiplexed Immunological Assay on Micro-Ring Resonators for Detection of Brain Injury-Specific Biomarkers
Sep 07 – Mar 10	Crawford, Fiona/ Rosamp Instit	Proteomic Analysis of Biomarkers and Pathogenesis of Traumatic Brain Injury
Sep 10 – Aug 13	Dambinova, Svetlana/ Kennesaw State Univ	Validation of AMPK Receptor Peptide Assay to Improve Diagnostic Certainty of mTBI
Oct 10 - Sep 13	Dash, Pramod K./ UT Houston	Biomarkers Prognostic for Elevated Intracranial Pressure
Jan 09 – Feb 14	Fedoroff, Howard/ Georgetown	Discovery and Validation of Peripheral Biomarkers of Traumatic Brain Injury
Jun 09 – Jun 13	Gary Kamimori/ WRAIR/ Geneva	Brain Injury Biomarkers and Behavioral Characterization of mTBI in Soldiers Following Repeated, Low-Level Blast Exposure
Sep 10 – Sep 13	Genovese, Raymond/ WRAIR	Neurocognitive and Biomarker Evaluation of Combination mTBI from Blast Overpressure and Traumatic Stress
Oct 10 – Sep 11	Gunasekar, Palur/ NMRC	Identification and Characterization of Serum/Cerebrospinal Fluid Biomarkers Following Blast Trauma (mTBI) in Rats: Short-Term and Long-Term Impact
Jun 08 – Sep 10	Hood, Leroy/ Institute for Systems Biology	Brain-Region- and Cell-Type-Specific Transcripts for Informative Diagnostics
Apr 10-Mar 13	Ling, Geoffrey/ USUHS	An Anti-Inflammatory Approach to Diagnosis and Treatment of Combined PTSD and Mild TBI
Feb 10 – Jan 13	Maheshwari, Radha/ USUHS	Role of MicroRNAs in Mild Traumatic Brain Injury (TBI) and Post-traumatic Stress Disorder (PTSD): Identification of Biomarkers and Therapeutic Targets
Aug 05 – Jul 06	McAloney, Richard/ Lynntech, Inc	Rugged, Handheld, and Array-Based Traumatic Brain Injury Biomarker Biosensor
Sep 09 – Oct 10	Mourad, Pierre/ Univ of Wash	A non-invasive biomarker for intracranial pressure
Oct 10 – Sep 11	Mueller, Gregory P. USUHS	Discovery of Early Biomarkers in TBI by Identifying Protein Autoantigens
Oct 10 – Sep 11	Reinman, Jaques/ BHSAF/TATRC	Identification of Novel Protein Biomarkers Based on In Vivo Models of Traumatic Brain Injury
Apr 09 – Mar 12	Stackmann, Donna/ NMRC	Evaluation of Prospective Biomarkers for TBI in the Presence of Hemorrhagic Shock
Sep 08 – Sep 10	Wagner, Amy K./ Univ of Pittsburgh	Data Modeling Approaches for Biomarkers in Clinical Traumatic Brain Injury

Return

COL Dallis C. Hack M.D./MCMR-RTC (301-619-7551) (DSN 343-)/ dallas.hack@us.army.mil UNCLASSIFIED Slide 45 of 28 3 August 2011

Update on Non-Invasive TBI Diagnostic Efforts

US Army MRMC

Dr. Douglas Gibson

In September 2010 BG James J. Carroll, USAF, signed a Capability Development Document (CDD) for a non-invasive traumatic brain injury diagnostic capability. This was the culmination of a procurement effort sponsored by USAF Air Combat Command. The CDD was taken up by Joint Program Committee 6 (JPC6) and in January of 2011 an Integrated Product Team (IPT) was chartered for joint development of a diagnostic device. This presentation will report on progress of that IPT. Included will be descriptions of the leading technologies.

Update

On

Noninvasive Neurodiagnostic

Product Development Effort

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Acronyms Used in this Briefing

The Problem

Mild Traumatic Brain Injury (mTBI) causes cognitive problems

The extent and severity of these problems is hard to assess

Those affected may

- have true recovery
- adapt to their deficits
- conceal their deficits
- be unaware of their own deficits (anosagnosia)

Current assessment relies largely on self-report and psychological tests

How Many People Have TBI?

Data are critical to understand traumatic brain injury (TBI) as an important public health problem. This data can help inform TBI prevention strategies, identify research and education priorities, and support the need for services among those living with a TBI

National TBI Estimates

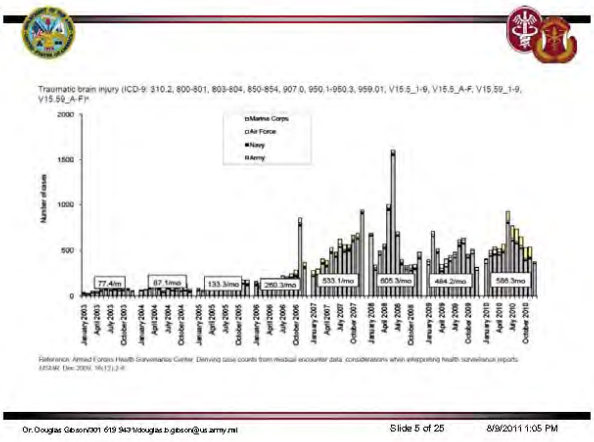
Each year, an estimated 1.7 million people sustain a TBI annually.[1] Of them:

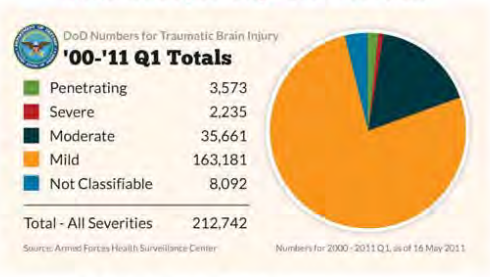
- 52,000 die,
- 275,000 are hospitalized, and
- 1,365 million, nearly 80%, are treated and released from an emergency department.

TBI is a contributing factor to a third (30.5%) of all injury-related deaths in the United States.[1]

About 75% of TBIs that occur each year are concussions or other forms of mild TBI.[2]

*This number of people with TBI who are not seen in an emergency department or who receive no care is unknown.





Mild TBI (mTBI) constitutes 77%

Return

Result

Because we cannot adequately assess mTBI

- Missions are impaired
- War fighters are imperiled
- Return to duty decisions cannot be adequately made
- Treatments cannot be developed
- Casualties cannot be accurately reported
- Service members (and families) suffer immediately and in the long term

Abstract

- In September 2010 BG James J. Carroll, USAF, signed a Capability Development Document (CDD) for a non-invasive traumatic brain injury diagnostic capability.
- This was the culmination of a procurement effort sponsored by USAF Air Combat Command and led by Col Mike Jaffee.
- The CDD was taken up by Joint Program Committee 6 (JPC6)
- December of 2010 Integrated Product Team (IPT) was chartered for joint development of a diagnostic device--Non-invasive Neurodiagnostic IPT (NN IPT)


NN IPT Membership
• General Membership:
➢ Dr. Douglas Gibson, CCCRP, IPT Chair
➢ Dr. Kenneth Curley, CCCRP, IPT Co-Chair and RAD Representative
➢ Mr. Michael Husband, USAMMA, IPT Co-Chair
➢ Ms. Leslie Connell, USAMMA, Logistics Representative
➢ Dr. Lloyd Salisbury, USAMMA, Product Manager
➢ Mr. Salmack, USAMMA, Clinical Technical Advisor Representative
➢ Ms. Cynthia Barlow, USAMRMC, Quality Management Representative
➢ Mr. Marcus Streips, USAMRMC, Legal Representative
➢ Mr. Terry Lee, USAMRMC, Testing
➢ Dr. Eugene Golanov, TATRC, Neuroscience Program Manager
➢ Dr. Christie Vu, CDMRP, Neuroscience Science Officer
➢ Dr. Kate Nassauer, MOMRP, JPC5/Concussion
➢ Mr. William Robertson, DCDD, User Representative
➢ Dr. Hank Gardiner, DCDD, User Representative
➢ COL Leo Tucker, DCDD, User Representative
➢ Dr. James Kirkpatrick, DCDD, Combat Developer
➢ Mr. Willie Lindsay, AMEDD Test Board, Field Evaluation
➢ Dr. Michael Russell, AMEDDC&S, Clinical Evaluation Representative
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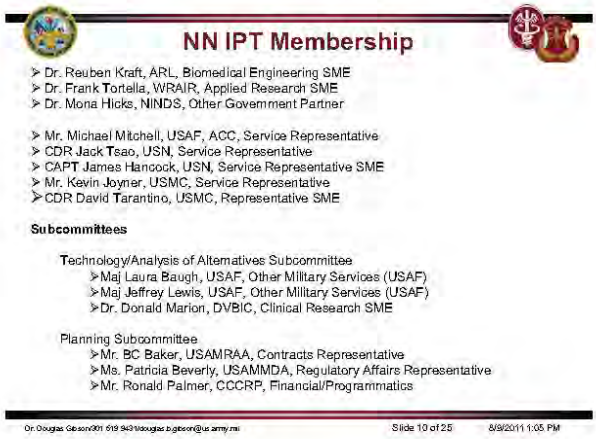
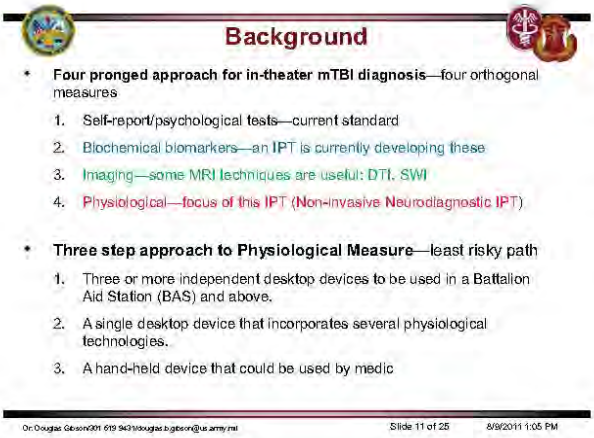
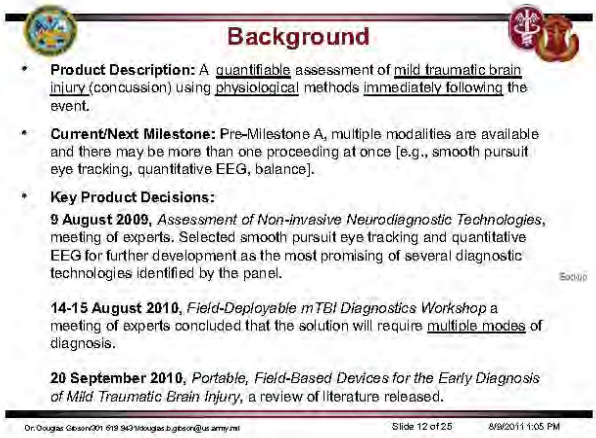

NN IPT Membership
➢ Dr. Reuben Kraft, ARL, Biomedical Engineering SME
➢ Dr. Frank Tortella, WRAIR, Applied Research SME
➢ Dr. Mona Hicks, NINDS, Other Government Partner
➢ Mr. Michael Mitchell, USAF, ACC, Service Representative
➢ CDR Jack Tsao, USN, Service Representative
➢ CAPT James Hancock, USN, Service Representative SME
➢ Mr. Kevin Joyner, USMC, Service Representative
➢ CDR David Tarantino, USMC, Representative SME
Subcommittees
Technology/Analysis of Alternatives Subcommittee
➢Maj Laura Baugh, USAF, Other Military Services (USAF)
➢Maj Jeffrey Lewis, USAF, Other Military Services (USAF)
➢Dr. Donald Marion, DVBIC, Clinical Research SME
Planning Subcommittee
➢Mr. BC Baker, USAMRAA, Contracts Representative
➢Ms. Patricia Beverly, USAMMDA, Regulatory Affairs Representative
➢Mr. Ronald Palmer, CCCRP, Financial/Programmatics
Slide 10 of 25


Background
• Four pronged approach for in-theater mTBI diagnosis—four orthogonal measures
1. Self-report/psychological tests—current standard
2. Biochemical biomarkers—an IPT is currently developing these
3. Imaging—some MRI techniques are useful: DTI, SWI
4. Physiological—focus of this IPT (Non-invasive Neurodiagnostic IPT)
• Three step approach to Physiological Measure—least risky path
1. Three or more independent desktop devices to be used in a Battalion Aid Station (BAS) and above.
2. A single desktop device that incorporates several physiological technologies.
3. A hand-held device that could be used by medic
Slide 11 of 25


Background
• Product Description: A quantifiable assessment of mild traumatic brain injury (concussion) using physiological methods immediately following the event.
• Current/Next Milestone: Pre-Milestone A, multiple modalities are available and there may be more than one proceeding at once [e.g., smooth pursuit eye tracking, quantitative EEG, balance].
• Key Product Decisions:
9 August 2009, Assessment of Non-invasive Neurodiagnostic Technologies, meeting of experts. Selected smooth pursuit eye tracking and quantitative EEG for further development as the most promising of several diagnostic technologies identified by the panel.
14-15 August 2010, Field-Deployable mTBI Diagnostics Workshop a meeting of experts concluded that the solution will require multiple modes of diagnosis.
20 September 2010, Portable, Field-Based Devices for the Early Diagnosis of Mild Traumatic Brain Injury, a review of literature released.
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Criteria used to rank technologies at 9 Aug 09 Assessment of Non-Invasive Neurodiagnostic Technologies Workshop

1. Can the proposed solution feasibly accomplish its diagnostic/monitoring purpose in a field environment? (including power requirements, environmental "noise" and human factors)
2. Will the technology substantially alter/improve management at echelons I, II or III as well as in transport? (Specify the levels at which the technology can be used)
3. Can the proposed technology be easily and quickly used by a medic, nurse, physician, surgeon or neurosurgeon? (specify level of provider required to use and interpret technology)
4. Can the technology be fielded in the time estimated by the investigator?
5. Is the unit cost reasonable?

Field-Deployable mTBI Diagnostics Workshop

14-15 August 2010

Cognitive Assessment--MACE, ANAM, ImPACT

Molecular biomarkers--Serum/blood biomarkers; peripheral white blood cell; gene expression; saliva; urine; microfluidics; nanotechnology

Imaging (vascular instability)--Transcranial Doppler; hemodynamic vascular analysis
Imaging (structural)--Transcranial ultrasound
Imaging (functional and structural)--Near-infrared imaging

Oculomotor--Saccades; smooth pursuit
Attention--Smooth pursuit eye tracking
Electrophysiology
Autonomic--Pupillometry; heart rate variability assessment
Vestibular--Balance error scoring system (BESS); Romberg; vestibulo-ocular reflex (VOR)

Cranial nerve function--Olfaction; oculomotor
Physical examination findings--Neurological soft signs—e.g. two-point discrimination; structured clinical interview

Portable, Field-Based Devices…

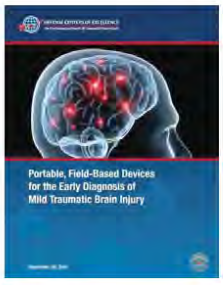
20 September 2010

Sensor Systems for Detecting Exposure to Injurious Events
Current Helmet-Based Sensor Systems

Neurocognitive/Psychological Testing Methods and Devices

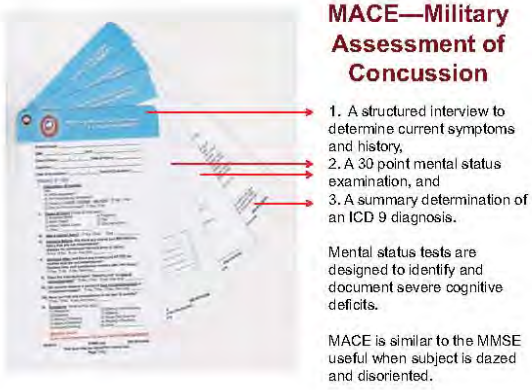
Point-of-Care Detection Devices for Assessing Biomarkers
Current State of Biomarkers for mTBI Diagnosis
Point-of-Care Biomarker Analysis Devices

Ocular Imaging Methods and Devices
Electrophysiologic Methods and Devices
Electroencephalography
Evoked Potentials and Event-Related Potentials
Electrical Impedance Methods and Devices
Sensory Assessment Methods and Devices
Olfactory System
Auditory System
Balance Assessment Methods and Devices
Transcranial Ultrasound Methods and Devices
Transcranial Doppler Ultrasound
Acoustical Imaging Methods and Devices
Passive Acoustical Monitors, Imaging Methods and Devices
Near-Infrared Spectroscopy



Directive-type Memo (DTM 09-033)

1. **Combat medic/Corpsman concussion (mTBI) triage (pre-hospital/no medical officer in the immediate area)—MACE used.**
2. **Initial provider management—MACE used.**
3. **Referral from Level I or II or polytrauma**
4. **Recurrent concussion (3 documented in 12 month span) evaluation—MACE used.**



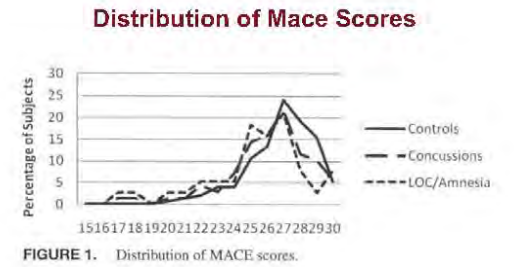


FIGURE 1. Distribution of MACE scores.

Results of a research study conducted in theater service members between 12 and 72 hours post-concussion and controls (Coldren, et al., 2010)

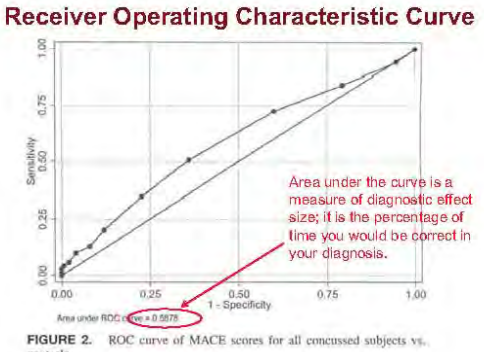
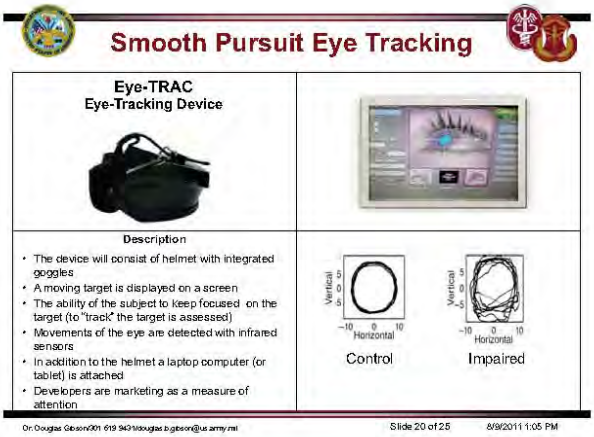
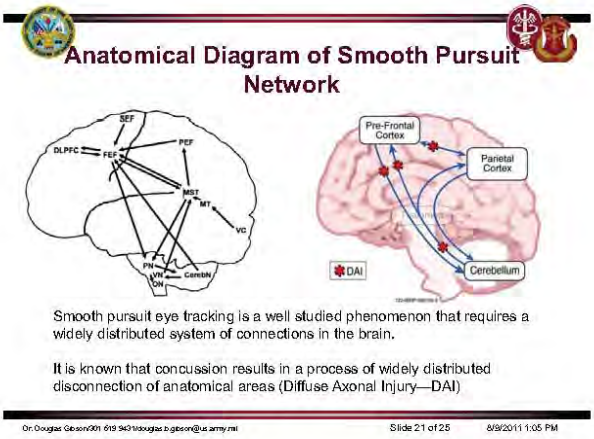


FIGURE 2. ROC curve of MACE scores for all concussed subjects vs. controls.




Anatomical Diagram of Smooth Pursuit Network
SEF
DLPFC
FEF
PEF
MST
MT
VC
PN
VN
DN
CerebN
Pre-Frontal Cortex
Parietal Cortex
DAI
Cerebellum
Smooth pursuit eye tracking is a well studied phenomenon that requires a widely distributed system of connections in the brain.
It is known that concussion results in a process of widely distributed disconnection of anatomical areas (Diffuse Axonal Injury—DAI)
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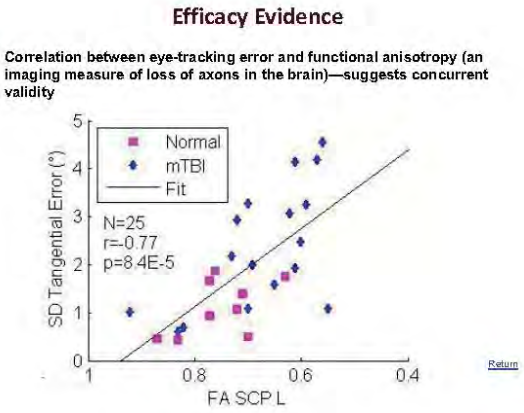
Efficacy Evidence
Correlation between eye-tracking error and functional anisotropy (an imaging measure of loss of axons in the brain)—suggests concurrent validity
Normal
mTBI
Fit
N=25
r=-0.77
p=8.4E-5
SD Tangential Error (°)
FA SCP L
Return


Lead Quantitative EEG Product
BrainScope
Ahead™ M-100
A portable, quantitative EEG platform
Description
The device will consist of a head mounted electrode array
Small electrical signals from the cortex of the frontal lobe of the cerebrum will be acquired
A hand-held processor will be attached to the electrode array
The processor will use a proprietary algorithm to analyze the data
Developers data indicates that mTBI patients can be distinguished from unimpaired individuals
Slide 23 of 25
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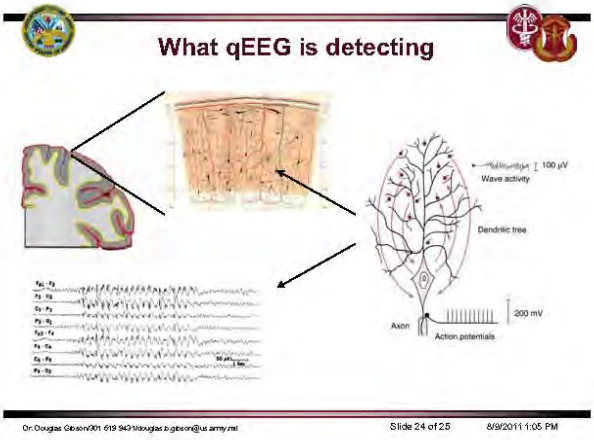
What qEEG is detecting
100 µV
Wave activity
Dendritic tree
200 mV
Axon
Action potentials
Slide 24 of 25
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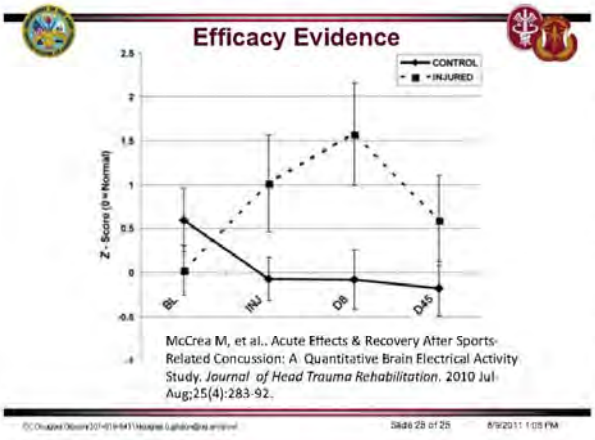
Efficacy Evidence
CONTROL
INJURED
Z - Score (0 = Normal)
2.5
2
1.5
1
0.5
0
-0.5
-1
BL
INJ
D8
D45
McCrea M, et al.. Acute Effects & Recovery After Sports-Related Concussion: A Quantitative Brain Electrical Activity Study. Journal of Head Trauma Rehabilitation. 2010 Jul-Aug;25(4):283-92.
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Acronyms Used in this Briefing
ACC—Air Combat Command
AMEDD—Army Medical Department
AMEDDC&S—Army Medical Department Center and School
ANAM—Automated Neuropsychological Assessment Metric
ARL—Army Research Laboratory
BAS—Battalion Aid Station
BESS—Balance error scoring system
BG—Brigadier General
CCCRP—Combat Casualty Care Research Program
CDD—Capability Development Document
CDR—Commander
DANA—Defense Automated Neurobehavioral Assessment
DCDD—Directorate of Combat and Doctrine Development
DoD—Department of Defense
DTI—Diffusion Tensor Imaging
DTM—Directive-type Memorandum
DVBIC—Defense and Veterans Brain Injury Center
EEG—Electroencephalography
ICD—International Statistical Classification of Diseases and Related Health Problems
ImPACT—Immediate Post-Concussion Assessment and Cognitive Testing
IPT—Integrated Product Team
JPC—Joint Program Committee
MACE—Military Acute Concussion Assessment
MMSE—Mini-Mental State Exam
MCMRP—Military Operational Medicine Research Program
mTBI—mild Traumatic Brain Injury
NINDS—National Institute of Neurological Disorders and Stroke
Q1—First Quarter
ROC—Receiver Operating Characteristic Curve
SME—Subject Matter Expert
SWI—Susceptibility Weighted Imaging
TATRC—Telemedicine and Advanced Technology Research Center
TBI—Traumatic Brain Injury
USAF—United States Air Force
USAMMA—US Army Medical Materiel Agency
USAMMDA—US Army Medical Materiel Development Activity
USAMRAA—US Army Medical Research Acquisition Activity
USAMRMC—United States Army Medical Research and Materiel Command
USMC—United States Marine Corps
USN—United States Navy
VOR—vestibulo-ocular reflex
WRAIR—Walter Reed Army Institute for Research
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Read out Loud: The Impact of Military Deployments on Shared Reading Practices in Pre-School Children

SAUSHEC

Capt Gayle Haischer-Rollo

Objective: The impact of a decade of military deployments on the population of military children is largely unknown. Parent-child reading habits during recent deployments may have long reaching impacts into the development of military children. Since September 11th 2001 many military families have experienced long and more frequent deployments. Although there are multiple ongoing studies investigating the psychosocial impact of deployments on families and children; there are few that focus on the important aspect of reading in the home. We decided to study the number of nights per week parents read to their children and compare the rates between military families with no deployed parents and those with one parent deployed. Methods: We distributed a brief questionnaire to 40 deployed and 70 non-deployed families at two similar southwestern military base clinics. Results: We found that parents with a deployed member in the family read to their children on average 4.65 nights a week and non-deployed 5.75 nights per week (p value 0.0059). We also found that families with a deployed member read on average 18 minutes per session as opposed to families with no deployed member reading 28.6 minutes per night (p value 0.0011). Conclusions: Health care professionals taking care of military dependants should be aware of that time spent in shared reading practices may be impacted during deployment. This information can be used when counseling parents and supporting them with resources aimed at increasing household literacy practices.

Read Out Loud

The impact of military deployments on shared reading practices in pre-school children

Gayle "Hava" Halscher-Rollo, MD
SAUSHEC

Background

- Early childhood literacy
  - Guides future attitudes
  - Better school preparedness

- Literacy rich environments
  - Advanced oral language
  - Higher reading knowledge and skills

Background

- Literacy poor
  - Parental attitudes
  - Low income
  - Minority
- 16% do not read to kids
  - 23% read 1-2x per week
- Parents factors
  - Time
  - Stress
  - Finances

*Shared Reading Practice-Benefits

- Rich, authentic, interesting literature can be used
- Provides opportunities to model reading for the children
- Opportunities for concept and language expansion
- Awareness of the functions of print, language patterns and word-recognition skills

*Holdaway, Don. 1979. *The foundations of literacy.*

Effect of Deployments

- Multiple on going studies since Sept 11th 2001

- Longer and more frequent deployments
- Long reaching social and emotional impacts
- Increased stress
  - Time
  - Finances

Study Design

- Cross Sectional Observational Study
  - Primary structured survey
    - Deployment status
    - Children ages
    - Nights per week/minutes per night
    - Demographic information

Recruitment

- Two Pediatric Clinics
  - WHMC
  - BAMC
- April to August 2010
  - Well children
  - Acute appointments
  - Letters offered

Inclusion/Exclusion Criteria

- Inclusion
  - Ages 0-5
  - One parent active duty
- Exclusion: Children of
  - Retirees
  - Civilians
  - Dependents

Data Analysis

- Number of days per week
  - Compare deployed vs. non-deployed with Mann Whitney
- Hours per night
  - Compare deployed vs. non-deployed with Mann-Whitney
- Demographics
  - Compare with Chi-Square or Mann-Whitney

Demographics

	Deployed	Non deployed	P-Value
Rank (n=110)			
<E5	22	28	1.88*
E6-E8	9	19	
01-03	3	15	
04-06	6	7	
Education (n=110)	1	1	0.074*
Some high school	9	4	
High school/GED	13	20	
Some college	12	33	
Graduated college	5	12	
Post graduate			

Demographics

	Deployed	Non deployed	P-Value
Race (n=110)			
Asian/Island Pacific	3	5	0.364
Black/African American			
Hispanic/Latino	3	11	
White/Caucasian	11	11	
	23	43	
Number of children in the household	2.1	2.0	0.504

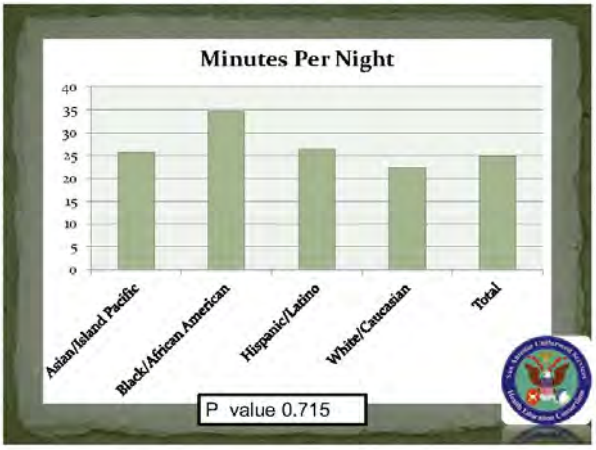
Demographics

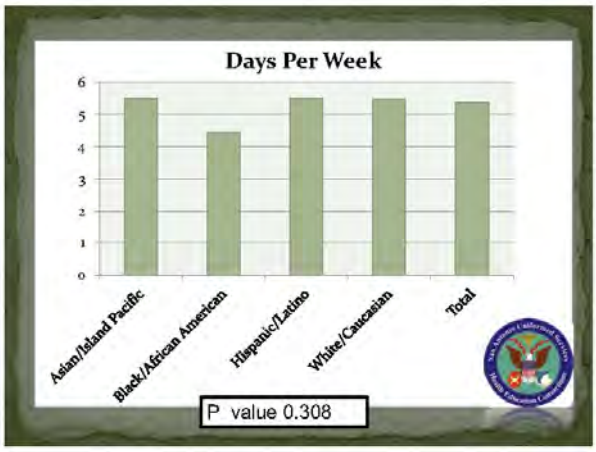
	Deployed	Non deployed	P-Value
Ages of Mothers	31.8	30.8	0.824
Ages of Fathers	32.7	32.8	0.354

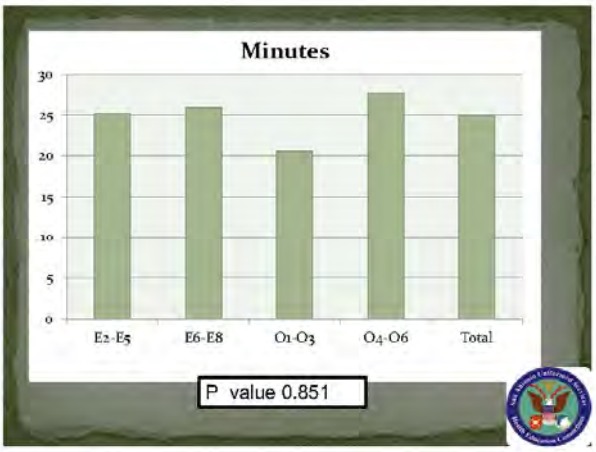
Results

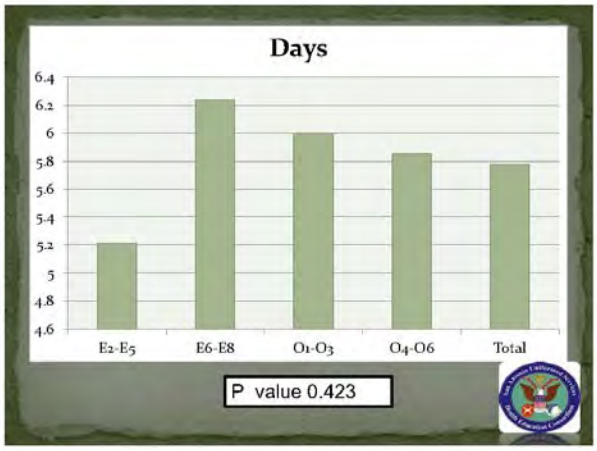
	Deployed	Non-Deployed	P-value
Avg. nights per week	4.65	5.75	0.0059*
Avg. minutes per night	18.3	28.7	0.0011**

*P < 0.01 = statistically significant









Summary of Results

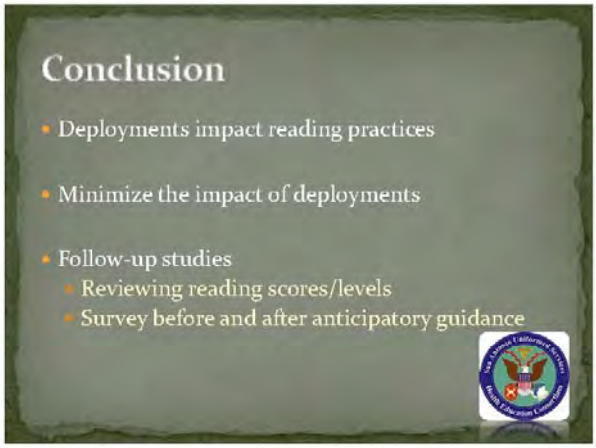
- No difference in reading with regards to
  - Race
  - Rank
- There is a difference in deployed and non-deployed
  - In days per week
  - In hours per day

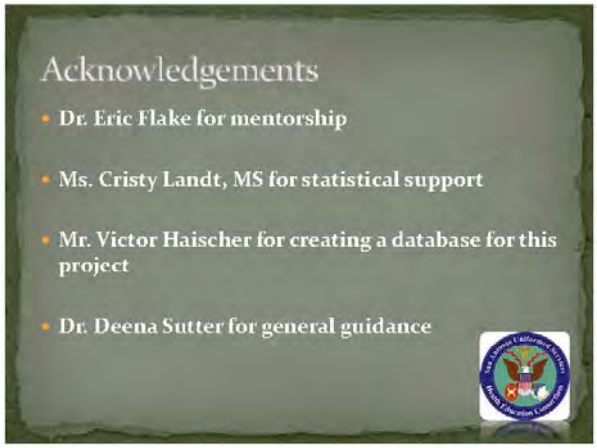
Discussion

- Many studies look at deployment effects
- Among the first to look at deployment effects on reading

Discussion

- Overall negative impact on time spent reading
- Information provides opportunity to provide
  - Resources
  - Anticipatory guidance
  - Information on the importance of reading


Conclusion
Deployments impact reading practices
Minimize the impact of deployments
Follow-up studies
Reviewing reading scores/levels
Survey before and after anticipatory guidance


Acknowledgements
Dr. Eric Flake for mentorship
Ms. Cristy Landt, MS for statistical support
Mr. Victor Haischer for creating a database for this project
Dr. Deena Sutter for general guidance


Questions?

Potential Burden of Repetitive Concussions in the Pediatric Population

633rd MDOS/SGOMP

MAJ Dalila Lewis

Sports injury is the second leading cause of traumatic brain injury in persons aged 15-24 years. Concussions are of particular interest in the pediatric population as the vast majority of persons playing contact or collision sports are under the age of 21 years. Young athletes are more prone to adverse sequelae following concussion according to an ever-growing body of scientific literature. Reasons for this are multiple, and include mechanical, physiologic, and neurometabolic differences of the developing brain. Suboptimal recovery in areas of attention, verbal memory, visual processing speed, reaction time, numerical sequencing ability, and learning has been observed via standardized computerized testing following concussion in young athletes. Further, post-concussive symptoms of headache, disequilibrium, emotional lability, dysregulated sleep, and cognitive difficulty are frequently prolonged after repeated concussions. Entities such as 'dementia pugilistica' and 'chronic traumatic encephalopathy' in adult athletes have highlighted concern regarding potential cumulative chronic neuropathologic changes that may result from repetitive concussive injury. In addition, current studies involving nuclear imaging to attempt to determine a temporal window of relative cerebral vulnerability following concussion have demonstrated prolonged disturbances in cerebral metabolism following concussive injury. Results of these studies have prompted the recommendation of a period of 'cognitive rest' following concussion ranging from one to several weeks. As persons taking care of both the active duty population and their young dependents, it is imperative that clinicians be aware of the potential impact of concussion, both immediate and long term.

Concussions in the Pediatric Population

Dalila Lewis, MD, FAAP
MAJ, USAF, MC
Staff Pediatric Neurologist
Naval Medical Center Portsmouth
Langley AFB

Outline

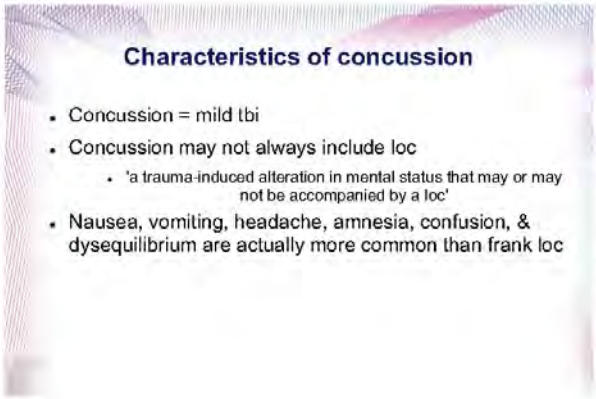
- Scope
- Scientific literature review
- Current management recommendations

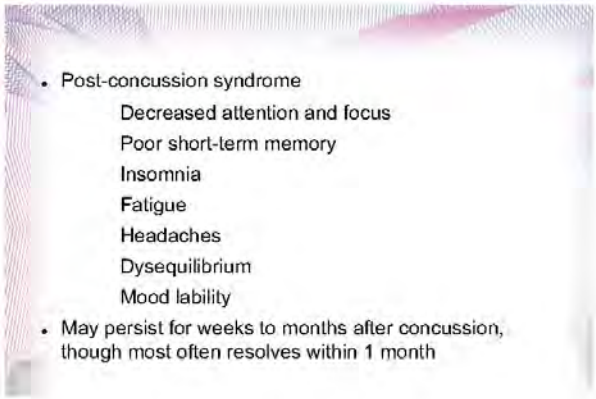
Scope

- Mva#1 cause, sports #2 cause
- 300K sports-related concussions annually
- >50% occur in persons under age 21y
- Sports participation increasing exponentially among youth

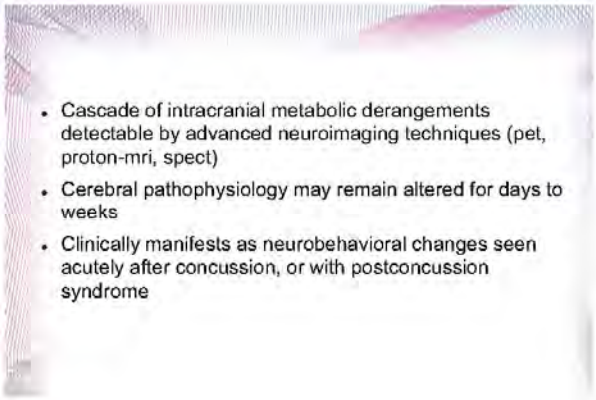
Problem

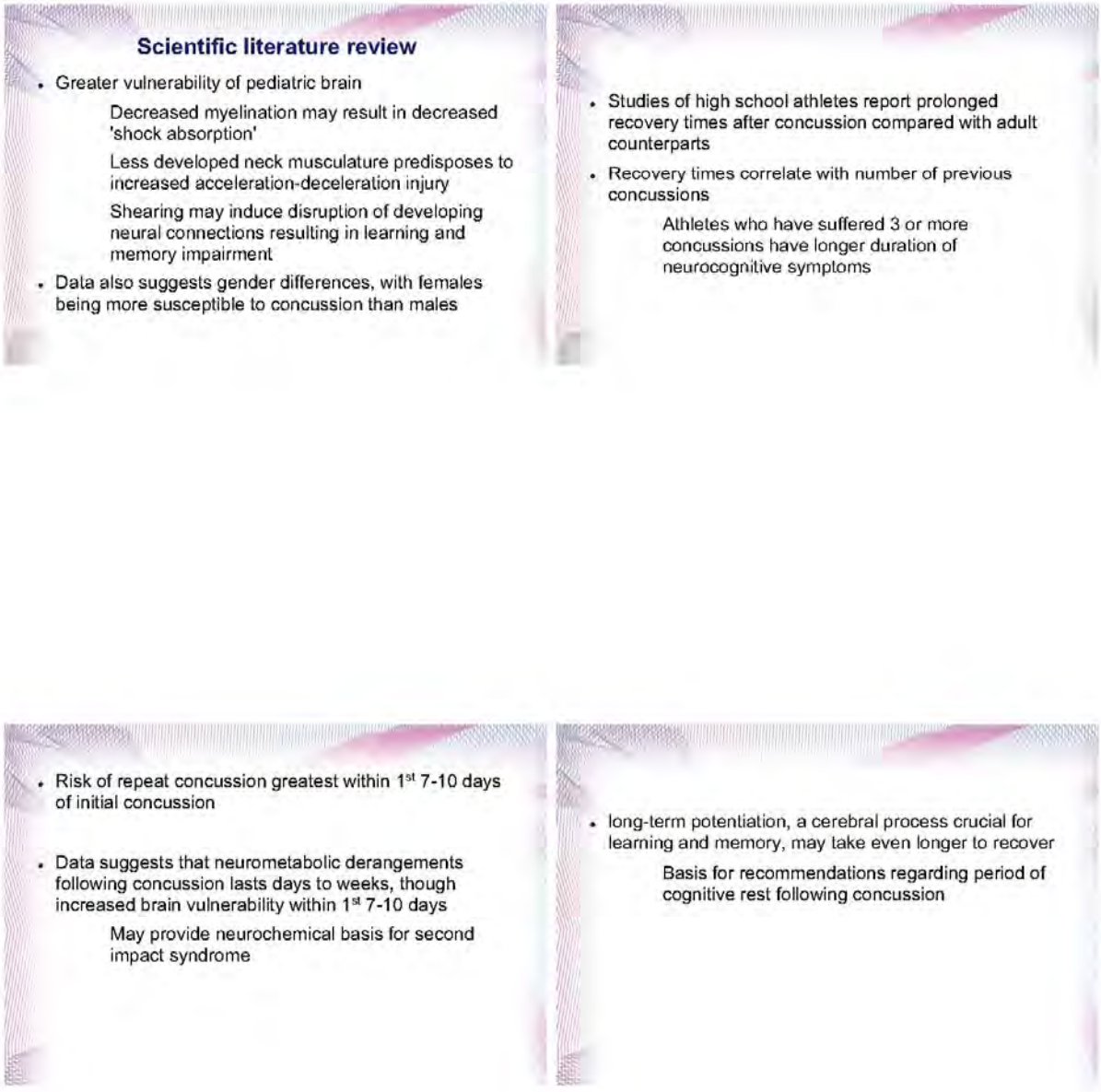
- Concussions are often under-recognized and under-reported
- Lack of understanding of neurobehavioral effects of concussion in lay population
- Multiple concussions predispose to longer recovery and negative cognitive sequelae


Characteristics of concussion
Concussion = mild tbi
Concussion may not always include loc
'a trauma-induced alteration in mental status that may or may not be accompanied by a loc'
Nausea, vomiting, headache, amnesia, confusion, & dysequilibrium are actually more common than frank loc


Post-concussion syndrome
Decreased attention and focus
Poor short-term memory
Insomnia
Fatigue
Headaches
Dysequilibrium
Mood lability
May persist for weeks to months after concussion, though most often resolves within 1 month


pathophysiology
No structural brain injury
normal conventional neuroimaging (ct, mri)
Concussion results in metabolic brain injury that is typically reversible
Increased cerebral glucose consumption
Decreased cerebral blood flow
Cerebral energy mismatch with decreased atp production
Increase in production of excitatory neurotransmitters


Cascade of intracranial metabolic derangements detectable by advanced neuroimaging techniques (pet, proton-mri, spect)
Cerebral pathophysiology may remain altered for days to weeks
Clinically manifests as neurobehavioral changes seen acutely after concussion, or with postconcussion syndrome


Scientific literature review
Greater vulnerability of pediatric brain
Decreased myelination may result in decreased 'shock absorption'
Less developed neck musculature predisposes to increased acceleration-deceleration injury
Shearing may induce disruption of developing neural connections resulting in learning and memory impairment
Data also suggests gender differences, with females being more susceptible to concussion than males
Studies of high school athletes report prolonged recovery times after concussion compared with adult counterparts
Recovery times correlate with number of previous concussions
Athletes who have suffered 3 or more concussions have longer duration of neurocognitive symptoms
Risk of repeat concussion greatest within 1st 7-10 days of initial concussion
Data suggests that neurometabolic derangements following concussion lasts days to weeks, though increased brain vulnerability within 1st 7-10 days
May provide neurochemical basis for second impact syndrome
long-term potentiation, a cerebral process crucial for learning and memory, may take even longer to recover
Basis for recommendations regarding period of cognitive rest following concussion

controversy

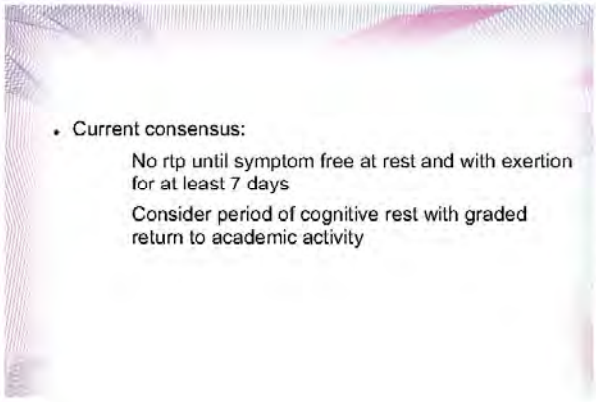
- Recent study of collegiate athletes found that a symptom-free waiting period ranging from 1-30+ days did not change outcome compared with control group
  - Same study notes that repeat concussions were greatest within 1st 10 days following initial concussion
  - Did not take into account history of prior concussions

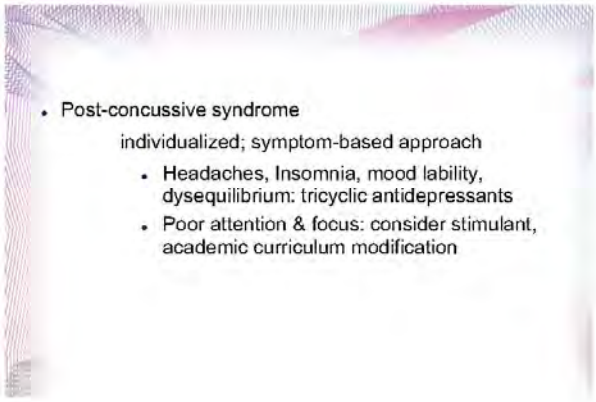
- studies also suggests repetitive concussions leads to greater risk for earlier-onset dementia
  - Chronic traumatic encephalopathy
- Genetic factors regarding vulnerability to brain injury may play a role

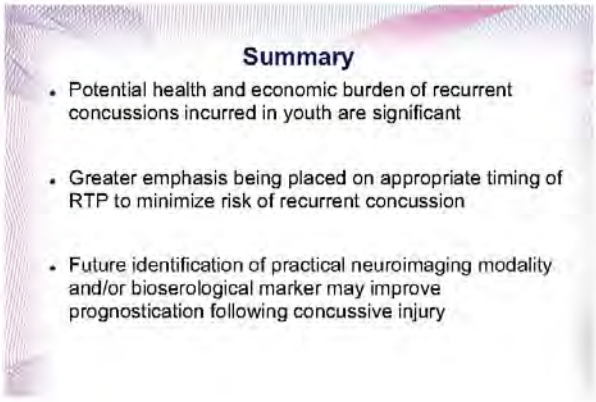
Current management & recommendations

- Currently, no serologic or radiographic marker commercially available to diagnose or monitor concussion resolution
- Purely clinical diagnosis, heavily reliant upon self-reporting of symptoms

- Diagnosis and treatment varies, based on community availability of resources
  - Computer-based neuropsychological testing (ImPACT, ANAM, Concussion Resolution Index, CogSport) prior to sports season and after concussion to aid in rtp decisions
  - Neuropsychology referral
  - Neurology referral
  - Sports medicine specialty referral


• Current consensus:
No rtp until symptom free at rest and with exertion for at least 7 days
Consider period of cognitive rest with graded return to academic activity


• Post-concussive syndrome
individualized; symptom-based approach
• Headaches, Insomnia, mood lability, dysequilibrium: tricyclic antidepressants
• Poor attention & focus: consider stimulant, academic curriculum modification


Summary
• Potential health and economic burden of recurrent concussions incurred in youth are significant
• Greater emphasis being placed on appropriate timing of RTP to minimize risk of recurrent concussion
• Future identification of practical neuroimaging modality and/or bioserological marker may improve prognostication following concussive injury

Concussion Research in Children and Youth

DCoE

Col Stephen Sharp

Concussion is receiving increased attention in the military and civilian populations because of the number of Service Members concussed in the Global War on Terror and the reports of long term cognitive issues after multiple concussions in professional sports such as the NFL. Even within the military community data has suggested that approximately 80% of concussion occurs CONUS from sports injuries and falls. Appropriately, increasing concern is being given to the effects of concussion on children and adolescents, particularly those stemming from athletic activities. A result has been an increased research effort looking for better ways to diagnose and assess concussion in young people, more stringent recommendations regarding returning to play, and better methods for treatment. Studies looking at biomarkers, EEG, and neuroimaging that were originally aimed at adults are now being investigated in youth as well. A recent controversial recommendation for cognitive rest after concussion has generated a lot of discussion. What is cognitive rest? Does outward cognitive rest equate to actual physiological brain rest? Are the results significant enough to warrant enforcing this on active young people? Additionally, researchers are looking at the question of the time that the brain is at risk post-concussion. How long should one be "protected" from a subsequent concussion? Should rules be changed for sports in youth that vary even more significantly from those in adults? The presentation will discuss the present reported research in these areas from screening and diagnosis through treatment and return to activity as they apply to children and youth.

DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

Concussion in Children and Adolescents: New Research; New Controversies

Stephen Sharp MD
Col, USAF, MC
Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury

Outline

- Epidemiology
- Issues in Pediatric/Adolescent Concussion
- Prevention
- Diagnosis
- Treatment

- Col Sharp has nothing to disclose.
- The opinions presented are those of the speaker and do not represent official positions of DCoE, the USAF or DoD.

Numbers???

- 1-1.5 million ED visits/year in US for TBI.
  - Roughly 80% for concussion (Ruff, 2009)
  - 91.5% of children treated and released from ED
- Reported around 300,000 sports related concussions per year. Estimates from 1.7-3.8 million (Lew, 2007)
- 8.9% of all sports injuries
- 65% of ER visits for sports-related TBI is in 5-18 y/o age group

Concerns

- Football has highest incidence of concussion
  - Appx 3 million children between 6-14 y/o play tackle football
- Girls have higher rates than boys in similar sports and often longer recovery times (Gessel, 2007; Gregory, 2007)
  - 68% more in soccer; 3 times as many in basketball
  - ? Weaker neck muscles and smaller head mass
  - ? Males less likely to report it

- "Youth are indestructible"
  - Previous thought was the developing brain was more resilient than older brain
  - Children often seem to recover more quickly
  - Newer research suggests the opposite- injuries to a developing brain may take longer to heal and may show signs of injury later
- Children's sports teams less likely to have trained staff on the sidelines for evaluations

Physiology

- Immature brain is more vulnerable to injury; metabolic changes present in the injured brain may alter child development. (Aloi, 2008)
  - Full cognitive maturity in mid-20's.
- Developing brain is 60 times more sensitive to NDMA and excitotoxic brain injury. (Field, 2003)
- Children commonly experience more severe symptoms of post-concussion syndrome. (McCrory, 2009)
- mTBI lesions tend to occur in WM, especially at the gray-white junction.
  - Depending on location have been associated with neuropsychiatric outcomes: ADD, OCD, anxiety disorder, etc. (Suskauer, 2009)

Grading

- The Management of Concussion in Sports. AAN, 1997.
  - Grades 1,2,3. Management based of grading.
- Zurich Statement. International Symposia on Concussion in Sports, 2008.
  - Delineation of "Grades" was arbitrary and not useful in managing concussion
- Sport-Related Concussion in Children and Adolescents. AAP, 2010.
  - Abandonment of previous grading scales for a symptom-based approach

Prevention

- Important part of preventing concussion. CDC "Heads-up" program (ie. helmets, mouth guards, etc)
  - Effectiveness difficult to measure in studies
  - Educational efforts at coaches especially important (Hollis, 2009)
- Soccer- protection from colliding heads, but not from heading the ball
  - Moving head vs. stationary head
  - Protects from soft-tissue injuries
- Football helmets decrease rate of concussion by roughly 1/3. ??? Repeated mild "bangs" to a developing brain.

Genetic testing

- Apolipoprotein E4 gene
  - E-4 allele associated with worse outcome after severe TBI; 3-9 fold increase in dementia
  - Concussion??; studies after mild/acute injury negative
- S-100 calcium binding protein gene
- Studies on children have not demonstrated significant differences in injury characteristics or outcomes; not recommended at this time.

Field Assessments

- Maddocks questions
- Standardized Assessment of Concussion (SAC)
- Balance Error Scoring System (BESS)
- Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)
- Sport Concussion Assessment Tool 2 (SCAT2)
  - Newest and combination of much of the above; not standardized for children as yet.
    - Ice hockey 9-17 y/o (Schneider, 2010)
- More beneficial to test > 15 minutes after cessation of exercise and in a standardized setting; not on the sideline

Neuropsychological testing

- Computerized test for athletes < 12 y/o in development
- Hand-held "do it yourself" concussion assessment

Biomarkers

- S-100 calcium-binding protein B
  - Elevated after all severities of TBI
  - No clear relationship to outcome in most studies
    - May help predict outcome with more severe TBI (Berger, 2007)
  - Influenced by age and time from injury (Aristotelis, 2010)
- Glutamate
  - Increased in children with cerebral contusion and chronic post-traumatic HA
- Neuron-specific enolase
  - Not discriminatory (Geyer, 2009; 2011)
- Glial fibrillary acidic protein (GFAP)
  - May have prognostic value after severe TBI (Fraser, 2011)
- Myelin basic protein
  - Not discriminatory (Simon, 2010)
  - May help predict outcome with more severe TBI (Berger, 2007)

Imaging: CT/MRI

- Easier and faster than MRI
  - < 4-8% positive in mTBI; < 0.5% require intervention. (Vasquez, 2007)
- Criteria for use
- Radiation exposure
  - About 2 rems; (20 chest X-rays). (Bazarian, 2006)
- ?MRI may be better after 48 hours
  - Up to 30% more sensitive
    - 10-57% abnormalities in mTBI (four studies, 1991-2004)
  - Susceptibility-weighted MRI
    - Shows promise in detecting hemorrhagic lesions (Beauchamp, 2011)

CHALICE Criteria

- The children's head injury algorithm for the prediction of important clinical events rule
- A computed tomography scan is required if any of the following criteria are present:
- *History*
  - Witnessed loss of consciousness of >5 min duration
  - History of amnesia (either anlegrade or retrograde) of >5 min duration
  - Abnormal drowsiness (defined as drowsiness in excess of that expected by the examining doctor)
  - ≥3 vomits after head injury (a vomit is defined as a single discrete episode of vomiting)
  - Suspicion of non-accidental injury (NAI, defined as any suspicion of NAI by the examining doctor)
  - Seizure after head injury in a patient who has no history of epilepsy
- *Examination*
  - Glasgow Coma Score (GCS)<14, or GCS<15 if <1 year old
  - Suspicion of penetrating or depressed skull injury or tense fontanelle
  - Signs of a basal skull fracture (defined as evidence of blood or cerebrospinal fluid from ear or nose, panda eyes, Battles sign, haemotympanum, facial crepitus or serious facial injury)
  - Positive focal neurology (defined as any focal neurology, including motor, sensory, coordination or reflex abnormality)
  - Presence of bruise, swelling or laceration >5 cm if <1 year old
- *Mechanism*
  - High-speed road traffic accident either as pedestrian, cyclist or occupant (defined as accident with speed>40 m/h)
  - Fall of >3 m in height
  - High-speed injury from a projectile or an object
- If none of the above variables are present, the patient is at low risk of intracranial pathology.

(Dunning, 2006)

Imaging: SPECT

- Children 2-18 with mTBI: medial temporal hypoperfusion was associated with persistent post-concussion syndrome

Imaging: Functional MRI

- Used serially to follow recovery and compensatory patterns
- Athletes with depression after TBI showed similar findings with non-athletes with major depression (Chen, 2008)
- Not much in children
  - Ongoing study at Univ of Toronto

Imaging: DTI

- Assess WM changes following DTI
- Adult studies:
  - Not associated with post-concussional disorder 2 months following mTBI
  - Acute changes can be seen following mTBI (McDonald, 2011)
- Changes seen in functional anisotrophy 6-12 months after mild and moderate TBI in children 10-18 (Wozniak, 2007)
- Some correlation with more intense post-concussion symptoms (Prabhu, 2011)
- Altered FA (suggestive of cytotoxic edema) within 6 days of injury in adolescents (Wilde, 2008)

Recovery times

- High school athletes demonstrated impairments of learning and memory up to 7 days post injury; compared to 3 days for college athletes.
- Return to play guidelines may need to be more conservative for younger athletes
- Cognitive impairment may begin or worsen several days after mild concussions that appeared to have rapid resolution (< 15 minutes)

Return to play

- Never on the same day
- Longer than college age and above
  - 7-10 days or longer

Education

- Education program for adults after TBI. At 3 months intervention group had fewer symptoms. (Ponsford, 2002)
- Similar results in pediatric study by same group (Ponsford, 2001)

Physical Rest

- Removed from activities with graded return
- High levels of overall activity may interfere with recovery; more moderate levels may be acceptable or beneficial. (Majerske, 2008)
  - Exercise to levels just below where symptoms are induced

Cognitive Rest

- Physical and cognitive rest mainstays of sports related concussion treatment
- Minimize activities that require concentration and attention: reading, schoolwork, TV, video games, text messaging, working online, playing games that require concentration
  - If phonophobia: cut down noise
  - If photophobia: sunglasses and a darkened room
- Academic performance based on memory and processing speed….
- Anecdotal studies

Medications

- Sleep
  - Melatonin
- Attention
  - Methylphenidate
    - Improvement in 5 attention tasks (Whyte, 1997)
    - Williams study: no help for pediatrics (Williams, 1998)

Medications

- Headache
- Cognition
  - Amantadine: Safe and well-tolerated in children and may improve cognition, but not statistically significant (Green, 2003; Beers, 2004)

Post-Concussion Syndrome

- Adult study: PCS in trauma patients does not show an association with mTBI (Meares, 2011)

Second Impact Syndrome

- Second, often minor, concussion leads to devastating injury or death
- CACNA1A calcium channel subunit gene may be associated
- Almost all have been in athletes 18 y/o or younger.

Conclusions…..

- A lot of research is underway in the area of concussion in children and adolescents
- There is not much "hard fact" data at this point
- Monitor symptoms rather than the concussion itself
- Error on the side of caution

- Questions????

Addressing Sleep Disorders Associated with Mild Traumatic Brain Injury

DCoE

CDR Michael Handrigan

Mild Traumatic Brain Injury is frequently associated with co-occurring sleep disturbances leading to difficulty in recovery, complications with rehabilitation and diminished quality of life. Sleep disturbances in the acute post-TBI period should be an important clinical focus since this is a period of active functional recovery. Identification and treatment of sleep disturbances during this period may reduce TBI morbidity, enhance recovery and limit long term sequelae of mTBI including the risk of chronic sleep disorder. This presentation will focus on the evaluation of sleep disorder following mTBI and treatment tips for sleep based on potential etiology.

DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

Mild Traumatic Brain Injury & Sleep Disorders

CDR Michael Handrigan, MD
Director, TBI Clinical Standards of Care Directorate
Defense Centers of Excellence for Psychological Health & Traumatic Brain Injury

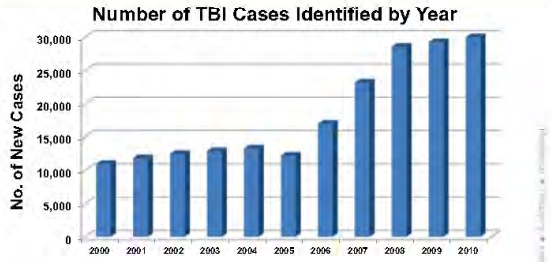
Sleep and the Military

- Consideration of sleep disturbances is particularly important for military service members
- Combat and support Service requirements often require long, unpredictable periods of wakefulness and sleep deprivation, which can impair human performance and vigilance
- The Military Deployment Survey of Sleep indicated that 74% of a group of deployed military personnel rated their quality of sleep as significantly worse in the deployed environment
- Service members with TBI may be at greater risk of sleep disturbances. Prevalence of sleep disturbances among military TBI populations range between **72% and 94%**
- Individuals with TBI and sleep disturbance are more likely to have deficits in key areas of cognitive functioning including attentional focus, memory recall and decision-making

(Himashree, et al., 2002; Lim & Dinges, 2008; Peterson, et al., 2008; Lew et al., 2010, 2007; Castriotta et al., 2007; Wilde et al., 2007)

2

How Big is the TBI Challenge?



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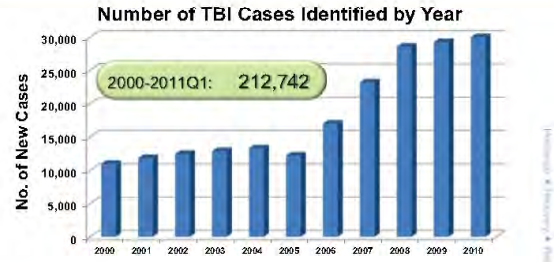
3

How Big is the TBI Challenge?



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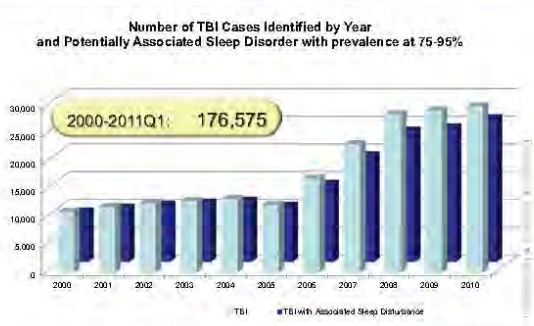
4

TBI with associated Sleep Disturbance



5

What We Know About Sleep and TBI

- TBI patients experience a spectrum of sleep disturbances following injury.
- There is a higher prevalence of sleep disturbances in the military
- The severity of TBI may play a role in the severity or prevalence of sleep disorders
- Dreaming is impaired temporarily following TBI, which may also be influenced by co-morbid conditions like PTSD.
- Well-established pharmacological therapeutics, such as modafinil and melatonin are beneficial.
- Non-pharmacological therapeutic approaches, such as cognitive behavioral therapy and sleep hygiene education, can be effective.
- Benzodiazepine hypnotics and antipsychotics should generally be avoided given their potential for impairment of neuronal recovery and cognitive performance.

6

Sleep and Human Physiology

Necessary for:
- cognitive processing
- cardiac function
- muscular enervation
- temperature regulation
- sexual function

Dysfunction leads to or exacerbates:
- Hypertension
- Obesity
- Diabetes
- Depression
- Stroke and heart attack
- Post-traumatic stress disorder
- Depression
- anxiety disorders

7

SLEEP and TBI

- Humans spend about a third of their lives in sleep
- Sleep is regulated by brain structures and mechanisms often affected by TBI.

8

Biology of Normal Sleep Mechanisms

- Non-rapid eye-movement (NREM)
  - NREM sleep is divided into three stages
  - each with unique physiological characteristics
- Rapid eye-movement (REM).
  - Dream state
  - 3-4 REM periods per sleep episode
  - 20-25% of total sleep time
  - critical component of memory consolidation
- Normal sleep patterns usually begins with NREM stage 1, then progresses through deeper NREM stages 2 and 3 until returning to stage 2 before proceeding into REM.

(Smith & Lapp, 1991; Vassalli & Dijk, 2009)

9

Sleep and Wakefulness Transitions

- Regulated by a two-process model
- Process S: promotes sleep
  - homeostatic drive for sleep
  - accumulates throughout the day
  - Peaks at night
- Process C: maintains wakefulness
  - Process C counteracts Process S
  - builds throughout the day and declines around bedtime

(Achermann, 2004; Saper, Lu, Chou, & Gooley, 2005; IOM, 2006).

10

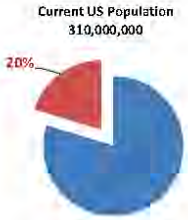
Sleep Disturbances and Sleep Disorders In the General Population

- Sleep Disturbance: any disruption of sleep
  - Complaint of poor sleep
  - Subjective sleep quality
  - Sleep Disorder: Medically recognized sleep disorders:
    - Insomnia
    - Hypersomnia
    - Narcolepsy
    - obstructive sleep apnea (OSA)
    - Circadian rhythm sleep disorder (CRSD)
- Classification systems include
  - International Classification of Sleep Disorders, Second Edition (ICSD-2)
  - American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders IV-TR* (Revised 4th ed.)
  - World Health Organization's International Classification of Diseases (ICD-9 and ICD-10).

11

General Sleep Disorder Prevalence

- 50 to 70 million Americans suffer from chronic sleep disorders, with negative consequences to their daily function and general health



(IOM, 2006; U.S. Census Bureau)

12

Insomnia

- Difficulty in initiating sleep or staying asleep
- Non-restorative sleep for at least one month
- Often accompanied by daytime fatigue or impairment in functioning.
- Effects approximately 33% of U.S. adult population
- Commonly associated with chronic stress on the hypothalamic-pituitary-adrenal (HPA) axis [elevated cortisol and adrenocorticotropic hormone, hyperactive corticotrophin releasing hormone]
- Risk factors for insomnia: older age, female gender, family history, stressful lifestyle, medical and psychiatric disorders (especially depression), and erratic work schedules

- *Diagnosis*
  - Self-reports of sleep quality and duration
  - Medical and psychiatric histories
  - Sleep logs, actigraphy2 and ambulatory monitoring
  - Polysomnography (PSG)

(DSM-IV-TR; Zammit, 2007; Arnold-Bloom & Ruth, 1999; Bradley, et al., 1996; Roth, 2006; Roth & Roehrs, 2003; IOM, 2006; Ygenzas et al., 2001)

13

Hypersomnias and Excessive Daytime Sleepiness (EDS)

- Hypersomnia: excessive sleepiness for at least one month as evidenced by prolonged sleep episodes or EDS
- Primary
  - Narcolepsy
  - Idiopathic hypersomnia
  - Rare disorders such as Kleine-Levin syndrome
- Secondary
  - sleep apnea, sleep deprivation, CRSD
  - drug abuse, depression, head trauma, stroke, neurodegenerative disease
- Effects approximately **4% to 20%** of the general population

- *Diagnosis*
  - Symptom inventories and clinical evaluation
    - Epworth Sleepiness Scale (ESS)
    - Stanford Sleepiness Scale

(DSM-IV-TR; Pagel, 2009; Johns, 1991; Herscovitch & Broughton, 1981; Ohayon 2005)

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Narcolepsy

- Primary hypersomnia
- EDS
- Repeated sleep attacks
- Cataplexy (sudden, reversible loss of muscle tone during consciousness
- Intrusions of REM sleep into transitions between sleep and wakefulness
- sleep onset REM (SOREM)
- Effects approximately **0.045%** of the general population
- Frequently associated with brain tumors

- *Diagnosis*
  - Symptom inventories and clinical evaluation
    - Epworth Sleepiness Scale (ESS)
    - Polysomnography
    - Multiple Sleep Latency Testing (MSLT)

(DSM-IV-TR, 2000; Silber, et al. 2002; Ohayon, 2006; Peacock & Berry, 2010)

15

Obstructive Sleep Apnea (OSA)

- AKA: Breathing Related Sleep Disorder
- Caused by complete or partial airway obstructions during otherwise normal sleep respiration
- Interrupt sleep and reduce blood oxygenation
- Result in neurocognitive and cardiovascular effects
- **24% to 28%** of men and **9% to 28%** of women experience sleep apnea events that warrant treatment
- Risk factors include: obesity, male gender and increasing age

- *Diagnosis*
  - Medical history
  - physical exam
  - sleep study,
  - polysomnography

(Dempsey, et al., 2010; Young, et al., 2002; White, 2006)

16

Sleep Disorders in the TBI Population

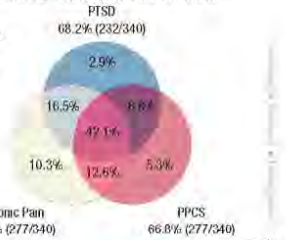
- **30% and 70%** of TBI patients experience sleep disturbances
- Sleep disturbances in TBI impacts attention and memory functioning
- The overlap depression and other anxiety disorders, suggests an increased risk for new or exacerbated psychological health disorders

(Orff, et al., 2009; Zeitzer, et al., 2009; Bloomfield, et al., 2010; Castriotta et al. 2007; Wilde et al., 2007)

17

Sleep Disorders Associated and the "Clinical Triad"

- Sleep disturbances appear to be particularly common in the military patient population and are associated with the "clinical triad" of TBI, PTSD and pain
- Sleep disturbances is seen in **93.5**% of this population.
- As many as **84**% of patients reporting mTBI symptoms also exhibit sleep disturbances
- TBI Patients with sleep disturbances required longer stays in acute trauma and rehabilitation units than TBI patients without sleep disturbances



(Lew et al., 2010, Lew et al., 2007)

18

Insomnia in TBI

- **50-71**% of TBI patients experience insomnia
- The presence of insomnia is associated with less severe injuries, more severe depressive symptoms, greater pain and greater fatigue.

(Ouellet et al., 2004; Ouellet & Morin, 2006)

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Hypersomnia and EDS in TBI

- Approximately **50%** of TBI patients experience hypersomnia and/or EDS
- PSG reveals significantly less time spent in REM sleep and significantly higher time spent in superficial NREM stage 2
- Reduced sleep efficiency in injured patients
- Significant daytime episodes of falling asleep, indicating EDS.
- Suggesting that that key brain structures involved in normal sleep, such as the brainstem, basal forebrain and hypothalamus may be affected in mTBI.

(Masel et al. 2001; Watson et al. 2007; Verma et al. 2007; Schreiber et al., 2008;

20

Narcolepsy and TBI

- **6%** of a TBI population in one study exhibited narcolepsy
- compared to **0.045%** in the general population

(Castriotta et al. 2007)

21

Sleep Apnea and TBI

- **23 – 47%** of adults with TBI exhibit evidence of sleep apnea within three months of injury as assessed by the Respiratory Disturbance Index (RDI).

(Webster et al. 2001; Young et al., 2002; Castriotta et al. 2007)

22

Impact of TBI on Dreaming and Nightmares

- Problems with dreaming are not typically a formal part of sleep disorder diagnosis
- studies suggest a transient reduction or cessation of dreaming following injury.
- Studies also suggest a relationship between TBI and Co-occurring psychological disorders.
- **56%** of veterans with mTBI in one study experienced sleep disturbances due to nightmare-induced awakenings associated with PTSD
- **83%** of veterans with mTBI and neurocognitive impairments experienced awakenings due to nightmares

(Farrams & Ver Beek, 1982; Ruff et al., 2008)

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Treatment of Sleep Disorders in TBI Patients
Insomnia

- **Pharmacological Treatment**
  - Hypnotics
    - Benzodiazepines **should be avoided** due to risk of dependence and rebound insomnia particularly due to potential interference with neuronal recovery
    - Non-benzodiazepine hypnotics (e.g., zolpidem, zaleplon, eszopiclone) may be acceptable alternatives
  - Antidepressants
    - TCA's (amitryptyline, desipramine, nortriptyline) may have a role in post-TBI depression, risk of overdose and suicide may be a significant concern
    - SSRI/ Serotonin Antagonists not well studied in TBI
  - Antipsychotics
    - Respiridone may improve insomnia and daytime sleepiness
    - But may also impair neuronal recover and cognitive performance
  - Melatonin Agonists
    - decrease sleep latency and increase sleep time
    - Studies not yet conclusive
- **Non-Pharmacological Treatment**
  - Cognitive behavioral therapy (CBT) and sleep hygiene psychoeducation
  - CBT alone may be more effective than pharmacological intervention alone or in combination with CBT

(Ranger, 2008; Zammit, 2007; Flanagan et al., 2007; Rao & Rollings, 2002; Zasler, 1993; Müller, 2005; Feinberg et al., 1982; Schreiber et al. 1998 Babcanec et al., 2010; Swoam & Mather, 2010; Wu , et al ,2008; Chesler & Morin, 2007)

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Treatment of Sleep Disorders in TBI Patients

Hypersomnia and EDS

- Hypersomnia and EDS are most commonly attributed to secondary causes
  - (e.g., sleep deprivation, OSA, CRSD, headaches, pain, other psychiatric and medical conditions)
  - Mainstay of treatment is to address the underlying cause
- **Pharmacological Treatment**
  - Modafinil 100 to 400 mg daily
    - Improved post-traumatic hypersomnia
    - Reported greater sense of attention
    - Effect may wane, thus may be best-suited as a short-term treatment solution
  - Prazosin
    - Improvement in post concussive headache, improved restful sleep and decrease in nightmares
  - Other medications for inducing alertness
    - amphetamines such as methylphenidate and dextroamphetamine
- **Non-Pharmacological Treatment**
  - sleep hygiene counseling in addition to oral prazosin
    - 100% reported improvement

(Wise, et al., 2007; Pagel, 2009; Castriotta et al., 2009; Ruff et al., 2009

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Treatment of Sleep Disorders in TBI Patients

Narcolepsy

- **Pharmacological Treatment**
  - Stimulants (e.g., amphetamines and methylphenidate)
    - promote alertness during the day
  - Modafinil
    - MSLT scores have improved with modafinil 200 mg daily
    - indicated for use in narcolepsy associated with EDS
- **Non-Pharmacological Treatment**
  - Management of narcolepsy in the general population typically relies on pharmacologic treatments.
  - Existing non-pharmacological approaches include sleep (i.e., nap) scheduling
  - managing social factors between the patients and their environment

(Peacock & Bonca, 2010; Thorpy, 2007; Wise et al., 2007; Kumar, 2008; Castriotta et al., 2009; Garma & Marchand, 1994)

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Treatment of Sleep Disorders in TBI Patients

Obstructive Sleep Apnea

- **Pharmacological Treatment**
  - The development of pharmacological treatments for OSA is fairly limited
  - Modafinil is FDA approved for OSA patients experiencing EDS despite optimal use of CPAP
- **Non-Pharmacological Treatment**
  - Continuous Positive Airway Pressure (CPAP) is the most common treatment for OSA in the general population.
    - However, patient adherence to CPAP is low so oral appliances and surgical options are also available.
    - CPAP significantly improved Apnea-Hypopnea Index (AHI) scores and significantly increased REM sleep

(Kumar, 2008; Weaver & Sawyer, 2009; Castriotta et al., 2009; Almeida & Lowe, 2009; Maurer, 2009)

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Complex relationships between mTBI and psychological health

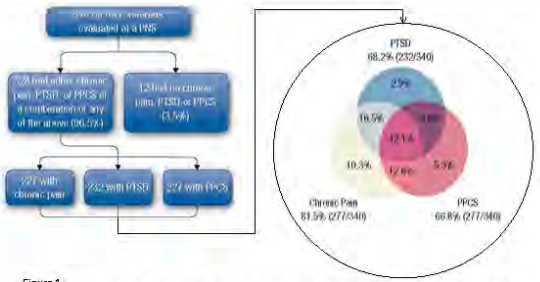

Figure 1.
The polytrauma clinical triad: Distribution of patients with chronic pain, posttraumatic stress disorder (PTSD), and persistent post-concussive symptoms (PPCS) in a sample of 340 Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) veterans evaluated at Department of Veterans Affairs Boston Polytrauma Network Site (PNS).

28

Existing CPGs to assist providers

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The Toolkit

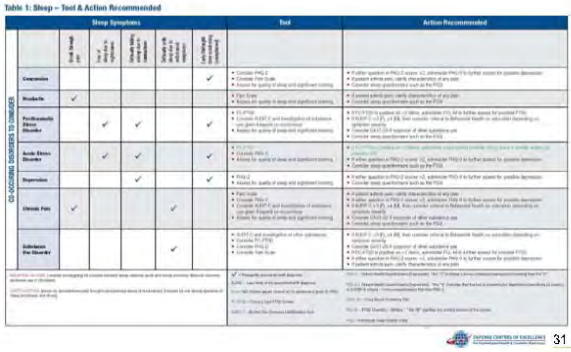
- Background
- The First Appointment
- How to Use this Guide
- Topics
- Appendix 1: Meds
- Appendix 2: Patient Education
- Appendix 3: Provider Resources

- Sleep
- Mood
- Attention
- Chronic pain
- Concussion
- Headache
- PTSD
- Acute Stress Disorder
- Depression
- Chronic Pain
- Substance Use Disorder

http://www.dcoe.health.mil/ForHealthPros/TBIInformation.aspx

30

Sleep Disorder tab



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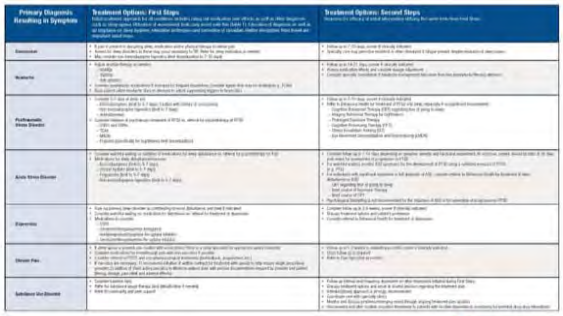
Sleep Disorder tab



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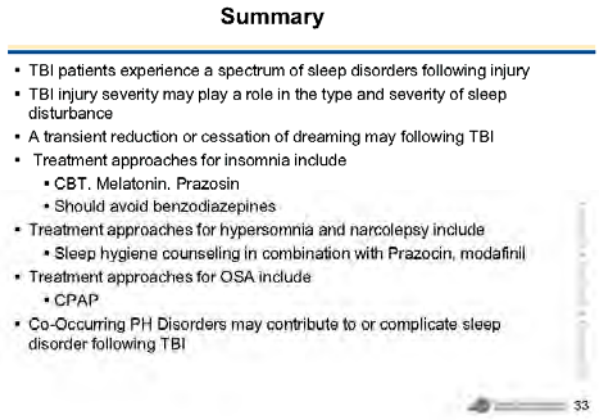
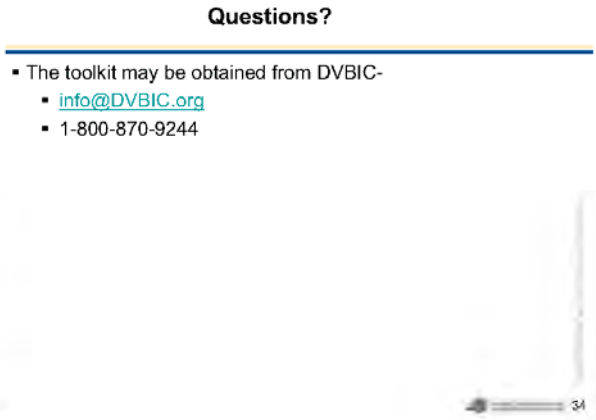

Summary
TBI patients experience a spectrum of sleep disorders following injury
TBI injury severity may play a role in the type and severity of sleep disturbance
A transient reduction or cessation of dreaming may following TBI
Treatment approaches for insomnia include
CBT. Melatonin. Prazosin
Should avoid benzodiazepines
Treatment approaches for hypersomnia and narcolepsy include
Sleep hygiene counseling in combination with Prazocin, modafinil
Treatment approaches for OSA include
CPAP
Co-Occurring PH Disorders may contribute to or complicate sleep disorder following TBI
33


Questions?
The toolkit may be obtained from DVBIC-
info@DVBIC.org
1-800-870-9244
34

The Association of Post-Deployment Symptoms with Concussion and Post-Traumatic Stress Disorder in US Soldiers Deployed to Iraq or Afghanistan

WRAIR

Dr. Richard Herrell

We examined the effects of single and multiple concussions on post-deployment health symptoms in a sample of 2,064 U.S. Soldiers who completed an anonymous survey 4 to 6 months after returning from deployment to Iraq or Afghanistan. 17% of the study participants reported suffering a concussion during their previous deployments. One third reported a head injury with a loss of consciousness (LOC), the remainder an alteration of consciousness (AOC) only. Of those reporting a concussion, 59% reported more than one concussion during their previous deployment. After adjustment for PTSD, depression, and other factors, LOC was significantly associated with headaches, memory problems and balance problems. However, PTSD and depression had a stronger association with these symptoms than concussion history. Multiple occurrences of concussion increased the risk of headache and sleep disturbances compared to a single occurrence, independent of PTSD or depression. However, even in this group, depression showed equivalent odds ratios for the association with headache and sleep disturbances. These data indicate that current screening tools for mTBI being used by the Department of Defense and Veterans Affairs may have limited utility in identifying individuals who have post-deployment symptoms uniquely attributed to concussions. Accumulating evidence supports the need for multidisciplinary collaborative models of treatment in primary care to address the full spectrum of post-war physical and neurocognitive health problems.

[Presentation slides not provided]

VA Screening and Evaluation Data for TBI: Effects of Psychiatric Symptoms and Injury Characteristics

DCoE / VA Maryland Health Care System

Dr. Alison Cernich

This presentation will summarize findings from a retrospective analysis of traumatic brain injury (TBI) screening and evaluation data from a VA Medical Center in an urban area. Data taken from the initial two years of the program were gathered to determine the effect of concurrent report of psychiatric symptoms on TBI symptom reports, the factor structure of the secondary level symptom questionnaire and the effect of concurrent psychiatric symptoms on the measure, and the effect of injury characteristics and psychiatric symptoms on neurocognitive evaluation. Sample size ranged from approximately 300 Veterans for the screening evaluations to 30 veterans who had data available from a neuropsychological evaluation. Findings from this retrospective review revealed that individuals with positive TBI and positive PTSD initial screens had higher rates of symptom reporting with greater emphasis on cognitive symptom reporting (eta squared = .061-.111). Screening data for depression accounted for the greater proportion of the variance in TBI symptom reporting, over and above PTSD or reported alcohol abuse. Finally, a smaller study of cognitive testing looked at the effect of PTSD and reported LOC on cognitive testing results. Self-reported LOC had a small effect on processing speed and there was no particular effect of PTSD on anything but symptom reports. Implications of these data for the evaluation of these Veterans and the need for close integration of rehabilitation and mental health services will be discussed.

VA SCREENING & EVALUATION DATA FOR TBI

Effects of psychiatric symptoms and injury characteristics

ALISON N. CERNICH, PH.D., ABPP-CN
ACTING VA SENIOR LIAISON
OFFICE OF REHABILITATION SERVICES
VETERANS HEALTH ADMINISTRATION
CO-AUTHORS: SHIRA KURTZ, PH.D., JESSICA CLARK, PH.D., & LAUREN CHANDLER, PH.D.

VA TBI SCREENING AND EVALUATION PROTOCOL

- Clinical Reminder System
- TBI Clinical Reminder
  - 4 question screen
  - Given to every returning OEF/OIF veteran who seeks services within the VA
- TBI Secondary Evaluation
  - *Neurobehavioral Symptom Inventory (NSI)*
  - Given to any veteran who screened positive on the primary screen
- Often then referred for further assessment

FACTOR STRUCTURE OF THE NSI

- Analyses of PCS symptom factors in civilian populations generally suggest the presence of three symptom clusters: cognitive, affective, and somatic (Axelrod et al., 1996; Potter, Leigh, Wade, & Fleminger, 2005)
  - Several studies show evidence of a fourth factor, comprising sensory (Cicerone & Kalmar, 1995) or behavioral symptoms (Ayr, Yeates, Taylor & Brown, 2009).
- Benge, Pastorek, and Thornton's (2009) analysis of the factor structure of the NSI in a veteran population revealed the presence of four factors: emotional disturbance, headaches, sensory problems, and a combination factor (sensory, cognitive, and motoric symptoms)
  - After controlling for symptoms of PTSD, the factor structure more closely resembled the three-factor structure seen in the civilian literature (e.g., cognitive, affective, and somatic symptoms), suggesting that PTSD symptoms appear to impact the presentation of PCS.

METHODS FOR FACTOR ANALYTIC STUDY

Study Overview

- A retrospective medical record review was conducted of OEF/OIF veterans who screened positive for mTBI on the Traumatic Brain Injury Screening Questionnaire administered to all returning service members in an urban VA Medical Center.
- Assessment protocol
  - PTSD screening and mTBI screening took place as part of a regular clinic visit.
  - At a follow-up evaluation, the veteran completed the 22-item Neurobehavioral Symptom Inventory (NSI) as a standard of care.
- Principal components analysis (PCA) was conducted using all 22 NSI items to determine factor structure. Parallel analysis of raw data (1000 permutations) was utilized to determine the number of factors to retain. Varimax rotations were used.
- Three separate PCA analyses were conducted to determine whether a positive PTSD screen impacted factor structure. The first included all participants, the second involved only those who screened positive for PTSD, and the third included only those who screened negative for PTSD.

Sample Characteristics
N = 299

	Participants	
	N	%
Age in Years	33.83±9.65	
Gender		
Male	271	90.6
Female	28	9.4
Ethnicity		
Caucasian	157	52.5
African-American	120	40.1
Hispanic	10	3.3
Asian/Pacific Islander	5	1.6
Unknown	7	2.3
PTSD		
Positive Screen	183	61.2
Negative Screen	116	38.8

NSI FACTOR STRUCTURE: RESULTS

- When all participants were included, two factors were retained, explaining a total of 50.9% of the variance (factor 1=42.96%; factor 2=7.94%).
- The first factor includes somatic symptoms and the second consists of both cognitive and affective symptoms.
- Four items did not load significantly onto either factor.
- When the PCA was conducted for those with and without a positive PTSD screen, results remained the same and only two factors were retained with similar factor loadings.

Factor 1 – Somatic	Factor 2 – Cognitive/Affective	No Significant Loading
Dizziness (.730)	Poor Concentration (.746)	Nausea
Loss of Balance (.771)	Forgetfulness (.678)	Hearing Difficulty
Poor Coordination (.636)	Difficulty Making Decisions (.720)	Sensitivity to Noise
Headaches (.515)	Slowed Thinking/Organizational Problems (.759)	Change in Appetite
Vision Problems (.674)	Fatigue (.612)	
Sensitivity to Light (.651)	Sleep Problems (.553)	
Numbness or Tingling (.502)	Anxious (.757)	
Change in Taste or Smell (.609)	Depressed (.743)	
	Irritability (.769)	
	Poor Frustration Tolerance (.799)	

EFFECT OF CO-OCCURRING DISORDERS

- The vast majority of patients who present to the clinic with a diagnosis of mild Traumatic Brain Injury (mTBI) do not often present with mTBI alone.
  - Of the veterans presenting to a Polytrauma Network Site in Lew's study (2009), 81.5% had more than one diagnosis and 42.1% had three co-occurring diagnosis including pain, posttraumatic stress disorder (PTSD), and post-concussion syndromes.
  - In another study by Ruff and colleagues (2008), approximately 66% of veterans presenting with headache and TBI had cognitive deficits on examination, more severe and frequent headaches, more reports of pain, higher rates of PTSD, and impaired sleep with nightmares.
- Veterans with positive TBI screens are more likely to have a diagnosis of PTSD, depression, and substance abuse disorder.
- The question addressed in the following data is how do these co-occurring disorders affect mTBI symptom reporting

POSTCONCUSSIVE SYMPTOMS: EFFECT OF CO-OCCURRING DISORDERS

- PTSD
  - A recent systematic review of the evidence found that for those with probable mTBI the frequency of co-morbid probable PTSD was 33-39% (Carlson et al., 2010).
  - Recent studies of individuals who have persistent symptoms following a mTBI suggest that the presence of PTSD may prolong the duration of symptoms and potentially exacerbate the severity of those symptoms (Polusney et al., 2011; Brenner et al., 2010; Thornton et al., 2009; Shneiderman, Braver, & Kang, 2008).
- Depression
  - Individuals with mTBI who experience depression post-injury report more symptoms and more severe symptoms than those mTBI patients without depression (Lange et al., 2010).
- Substance use
  - In a recently published study of active duty soldiers with mTBI, there was a slightly higher rate of alcohol abuse in individuals with a comorbid mTBI diagnosis compared to other injuries (6.9% v 4.4%). However, when other factors were controlled in a multivariate analysis, the relationship was not as strong (Heltemes et al., 2011).

VA PSYCHOLOGICAL HEALTH SCREENS

- Annual screens are conducted as part of regular clinical visits and include:
  - PTSD (PCL-2)
  - Depression (PHQ-2)
  - Substance abuse (CAGE)
  - Suicide

PTSD SCREENING & TBI SYMPTOM REPORTING

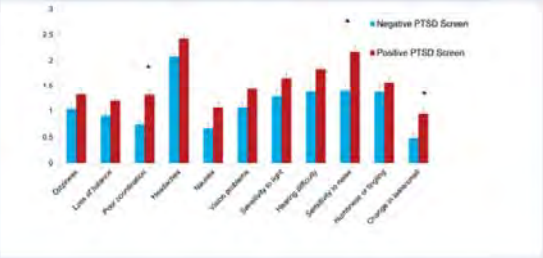
Objectives & Methods

- Objective: Determine the effect of a concurrent positive PTSD screen on report of post concussive symptoms
- Methods: Analyses of variance were conducted for all 22 items on the NSI to compare those with and without positive PTSD screens for differences in symptom reporting.

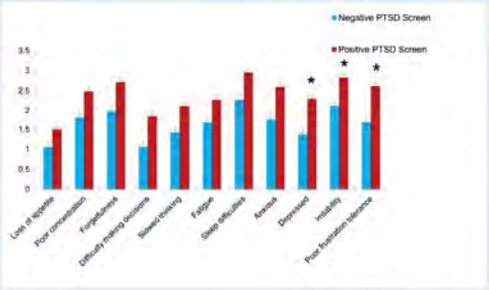
Sample Characteristics N = 252

	Participants	
	N	%
Age in Years	33.92 ± 9.82	
Gender		
Male	228	90.5
Female	24	9.5
Ethnicity		
Caucasian	136	54.0
African-American	97	38.5
Hispanic	9	3.6
Asian/Pacific Islander	4	1.6
Unknown	6	2.4
PTSD		
Positive Screen	153	60.7
Negative Screen	99	39.3

PTSD SCREENING & TBI SYMPTOM REPORTING: SOMATIC & NEUROSENSORY



PTSD SCREENING & TBI SYMPTOM REPORTING: COGNITIVE & AFFECTIVE

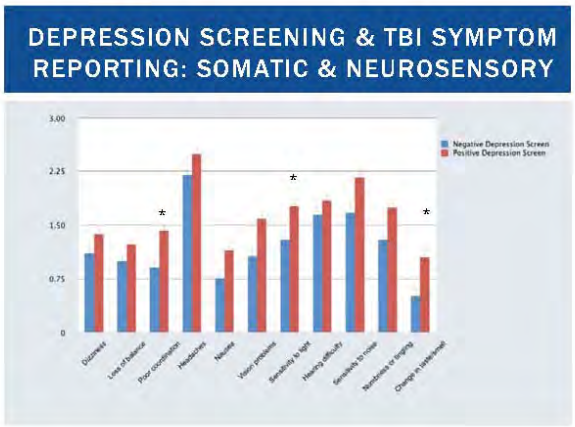


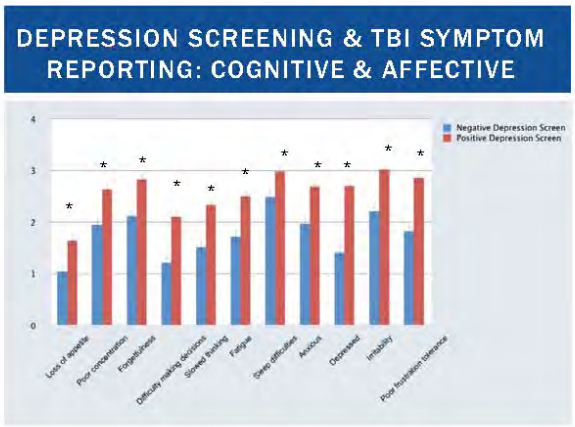
COMBINATION OF CO-OCCURING DISORDERS: EFFECT ON TBI SYMPTOMS

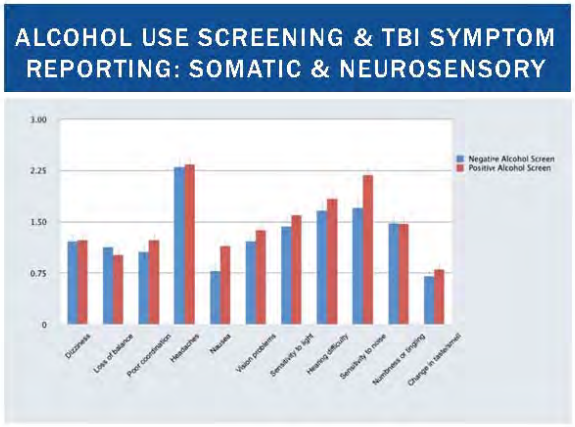
Study Objectives & Methods

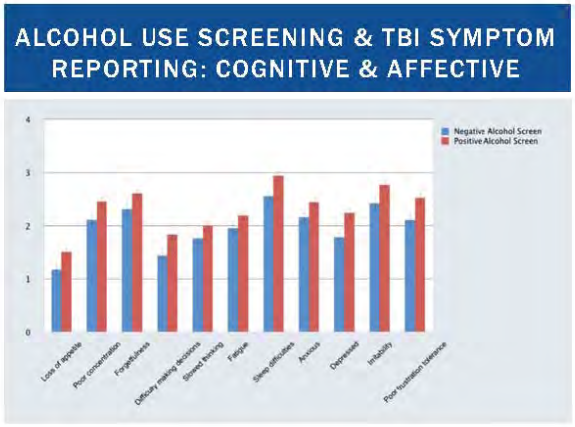
- The purpose of this study was to determine the effect of depression and substance use screens on TBI symptom reporting and to determine if the screening data from all behavioral health screens could be used to predict post-concussion symptom reporting.
- T-tests were used to evaluate group differences in symptom reporting on the NSI.
- Hierarchical multiple regressions were used to determine the relative contribution of each screen to post-concussion symptom reporting.
- Incremental F was used to determine whether the addition of a particular screening measure improved the predictive ability of the model.

Sample Characteristics N = 296


DEPRESSION SCREENING & TBI SYMPTOM REPORTING: SOMATIC & NEUROSENSORY
Negative Depression Screen
Positive Depression Screen
Dizziness
Loss of balance
Poor coordination
Headaches
Nausea
Vision problems
Sensitivity to light
Hearing difficulty
Sensitivity to noise
Numbness or tingling
Change in taste/smell


DEPRESSION SCREENING & TBI SYMPTOM REPORTING: COGNITIVE & AFFECTIVE
Negative Depression Screen
Positive Depression Screen
Loss of appetite
Poor concentration
Forgetfulness
Difficulty making decisions
Slowed thinking
Fatigue
Sleep difficulties
Anxious
Depressed
Irritability
Poor frustration tolerance


ALCOHOL USE SCREENING & TBI SYMPTOM REPORTING: SOMATIC & NEUROSENSORY
Negative Alcohol Screen
Positive Alcohol Screen
Dizziness
Loss of balance
Poor coordination
Headaches
Nausea
Vision problems
Sensitivity to light
Hearing difficulty
Sensitivity to noise
Numbness or tingling
Change in taste/smell


ALCOHOL USE SCREENING & TBI SYMPTOM REPORTING: COGNITIVE & AFFECTIVE
Negative Alcohol Screen
Positive Alcohol Screen
Loss of appetite
Poor concentration
Forgetfulness
Difficulty making decisions
Slowed thinking
Fatigue
Sleep difficulties
Anxious
Depressed
Irritability
Poor frustration tolerance

Incremental Effect of PTSD

Model	Stand. Beta	R	R Square	Adjusted R Square	Change Statistics: R Square Change	F Change	Sig. F Change
1	–	.415[a]	.173	.167	.173	30.542	.000
2	.168	.440[b]	.194	.185	.021	7.622	.006

Incremental Effect of Depression

Model	Stand. Beta	R	R Square	Adjusted R Square	Change Statistics: R Square Change	F Change	Sig. F Change
1	–	3.28[a]	.107	.101	.107	17.608	.000
2	.338	.440[b]	.194	.185	.086	31.238	.000

Incremental Effect of Substance Abuse

Model	Stand. Beta	R	R Square	Adjusted R Square	Change Statistics: R Square Change	F Change	Sig. F Change
1	–	.440[a]	.193	.188	.193	35.125	.000
2	-.014	.440[b]	.194	.185	.000	.063	.803

PREDICTION OF TBI SYMPTOM REPORTING

Overall all three screens accounted for 19% of variance with depression and PTSD having a significant unique contribution to overall scores.

EFFECTS OF PTSD & INJURY CHARACTERISTICS ON NEUROCOGNITION

Objectives & Methods

- Examine both the subjective complaints and objective cognitive scores on neuropsychological testing among a sample of veterans with diagnosed mTBI, some of whom had co-occurring PTSD diagnoses.
- Of veterans from the larger retrospective sample, 40 who had cognitive testing available were randomly selected for inclusion in this analysis. Only 28 of those selected were included in this study due to the presence of exclusion criteria.
- Neuropsychological testing and subjective complaints on the Neurobehavioral Symptom Inventory (NSI) were then compared for two sets of contrasts using one-tailed t-tests.

Sample Characteristics N = 28

40 Randomly Selected
↓
7 Lacked Evidence of TBI (17.5%)
↓
5 Failed Effort Testing (12.5%)
↓
1 Had Severe Brain Injury
↓
Total Sample for this Analysis = 28

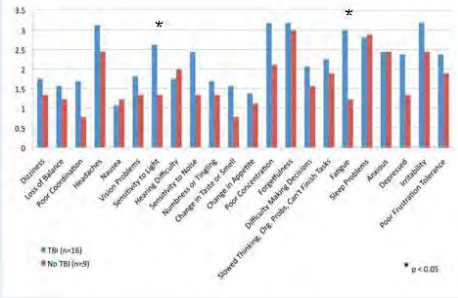
Age *M* = 23.32, SD = 7.26, Range = 23-48
Race: Caucasian (68%), African American (29%)
Men = 24 (85.7%); Women = 4 (14.3%)

Clark, J.R., Kim, S.W., & Daniels, A.S. (2011). Subjective complaints and neurocognitive performance in veterans from Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF). Poster presented at the meeting of the International Neuropsychological Society, Boston, MA.

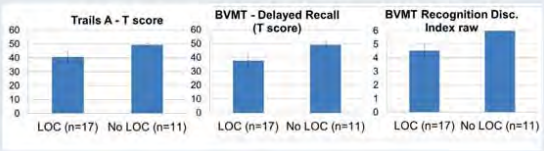
DOMAINS OF PERFORMANCE

Domain	Measure
Processing Speed	Trail Making Test – Part A
Attention/Working Memory	WAIS-III Digit Span
	WAIS-III Letter Number Sequencing
	Conners' Continuous Performance Test -II (CPT-II)
Learning & Memory	California Verbal Learning Test-II (CVLT-II)
	Brief Visual Memory Test-Revised (BVMT-R)
Executive Functioning	Trail Making Test – Part B

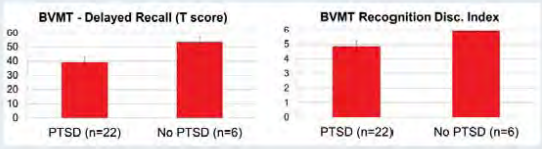
EFFECTS OF LOC ON SYMPTOM REPORTING



EFFECTS OF TBI ON COGNITIVE PERFORMANCE



EFFECTS OF PTSD ON COGNITIVE PERFORMANCE



SUMMARY AND DISCUSSION

- The factor structure of the symptom reporting measure may vary as a result of the population sampled and the presence of co-occurring disorders.
- The effect of psychological health symptoms on TBI symptom reporting may be dependent on the level of the measure used and the co-occurring conditions included as covariates.
- Depression seems to play an equally important role in the presentation of symptoms related to TBI as PTSD.
- Verification of TBI in clinical interview is an important factor in examining larger population data.
- PTSD and TBI seem to exert differential effects on cognitive performance in individuals referred for additional evaluation.

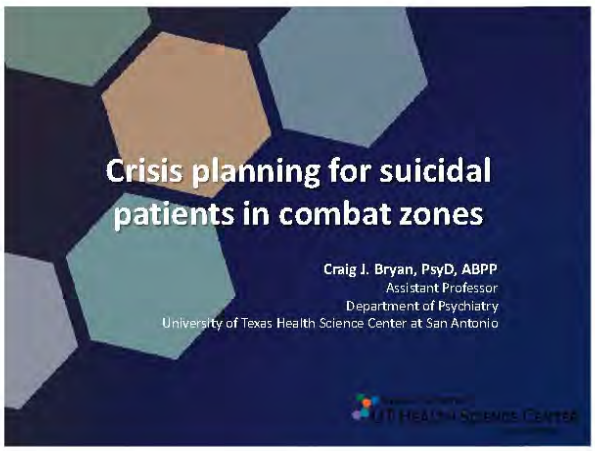
QUESTIONS?

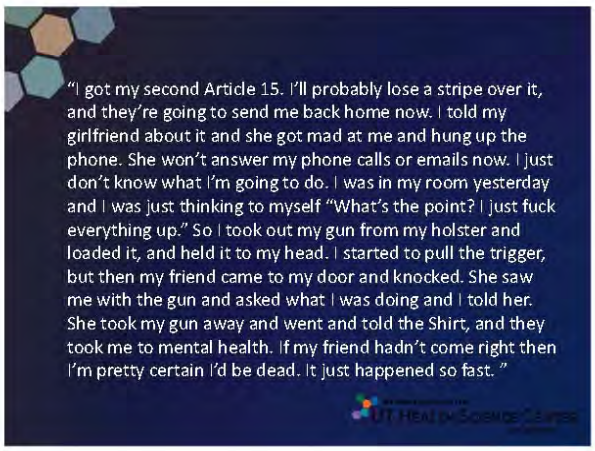
Crisis planning for suicidal patients in combat zones

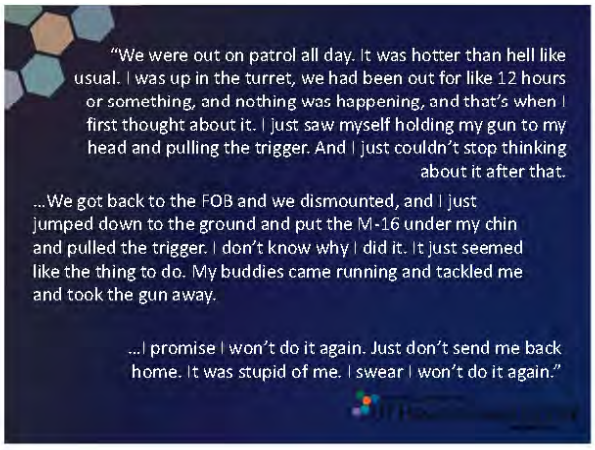
University of Texas Health Science Center at San Antonio

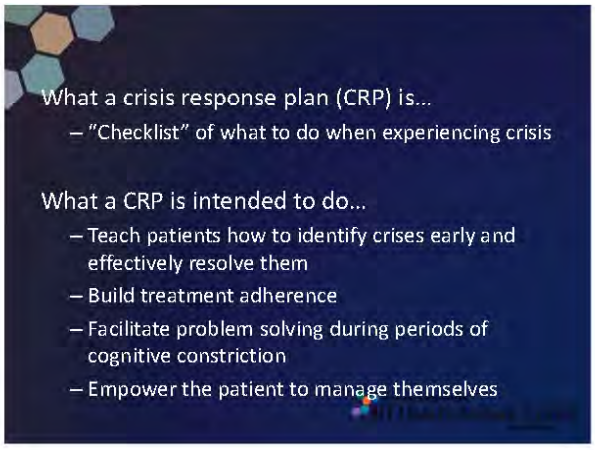
Dr. Craig Bryan

The crisis response plan (CRP) is an increasingly common intervention for the management of suicidal individuals across settings that has been transplanted to combat zones and aeromedical evacuation system. However, the effective use of CRPs within these settings can be hindered by contextual limitations. In the current presentation, real-life challenges and practical, evidence-based recommendations for the use of CRPs to maximize effectiveness of suicide risk management within combat zones and the aeromedical evacuation system are discussed.


Crisis planning for suicidal patients in combat zones
Craig J. Bryan, PsyD, ABPP
Assistant Professor
Department of Psychiatry
University of Texas Health Science Center at San Antonio


"I got my second Article 15. I'll probably lose a stripe over it, and they're going to send me back home now. I told my girlfriend about it and she got mad at me and hung up the phone. She won't answer my phone calls or emails now. I just don't know what I'm going to do. I was in my room yesterday and I was just thinking to myself "What's the point? I just fuck everything up." So I took out my gun from my holster and loaded it, and held it to my head. I started to pull the trigger, but then my friend came to my door and knocked. She saw me with the gun and asked what I was doing and I told her. She took my gun away and went and told the Shirt, and they took me to mental health. If my friend hadn't come right then I'm pretty certain I'd be dead. It just happened so fast."


"We were out on patrol all day. It was hotter than hell like usual. I was up in the turret, we had been out for like 12 hours or something, and nothing was happening, and that's when I first thought about it. I just saw myself holding my gun to my head and pulling the trigger. And I just couldn't stop thinking about it after that.
...We got back to the FOB and we dismounted, and I just jumped down to the ground and put the M-16 under my chin and pulled the trigger. I don't know why I did it. It just seemed like the thing to do. My buddies came running and tackled me and took the gun away.
...I promise I won't do it again. Just don't send me back home. It was stupid of me. I swear I won't do it again."


What a crisis response plan (CRP) is...
– "Checklist" of what to do when experiencing crisis
What a CRP is intended to do...
– Teach patients how to identify crises early and effectively resolve them
– Build treatment adherence
– Facilitate problem solving during periods of cognitive constriction
– Empower the patient to manage themselves

What a CRP is not…
- No suicide contract
- Contract for safety
- Behavioral agreement

Contracts and agreements typically dictate what the patient will not do when distressed, and restrict autonomy

Common CRP mistakes

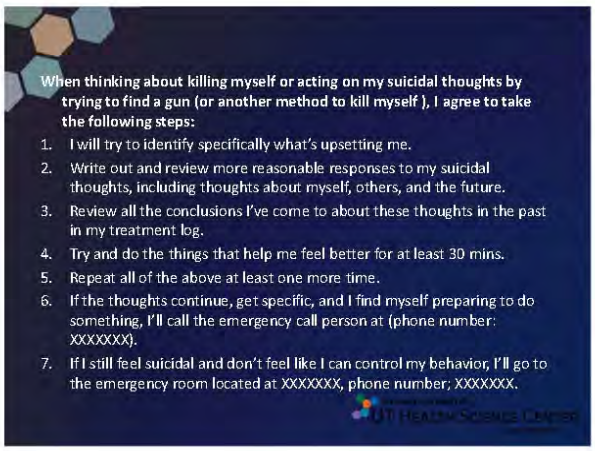
- Using xeroxed forms
- Overemphasis on external support
- Too vague and nonspecific
- Too wordy
- Not created collaboratively between patient and provider
- One-time intervention
- No skills training

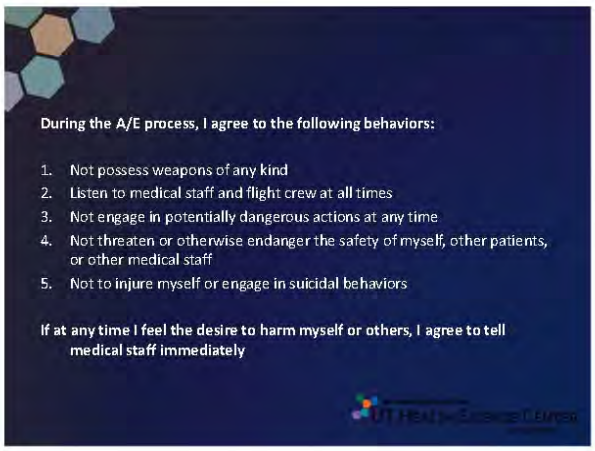
Common CRP mistakes in combat zones

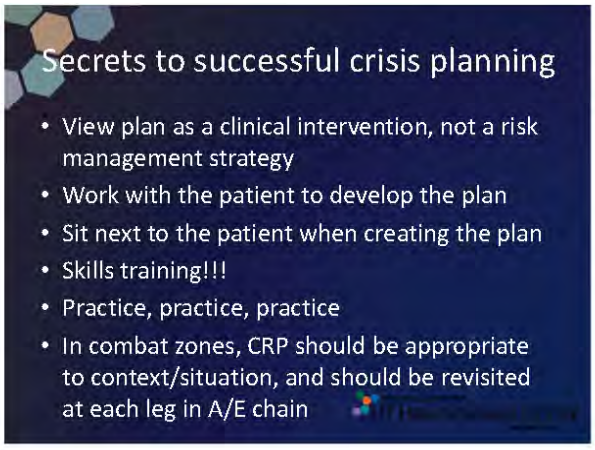
- Not adapted to contextual realities
  - Differences in availability of social support
  - Easy access to lethal means
  - Restricted ability to use common coping strategies (e.g., behavioral activation)
- Not responsive to different situational demands within A/E system

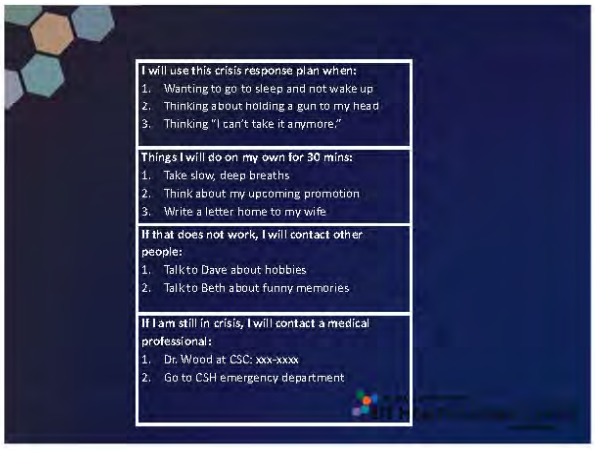
When thinking about killing myself or acting on my suicidal thoughts by trying to find a gun (or another method to kill myself), I agree to take the following steps:

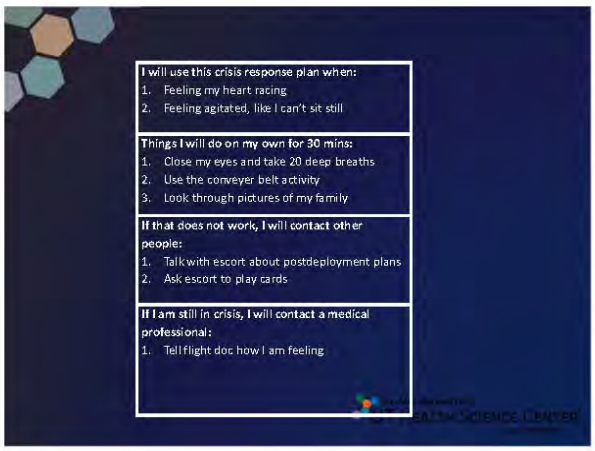
1. Call a friend or a family member to talk about what's bothering me.
2. Call my mental health provider at the clinic.
3. Go to the emergency department at the hospital.

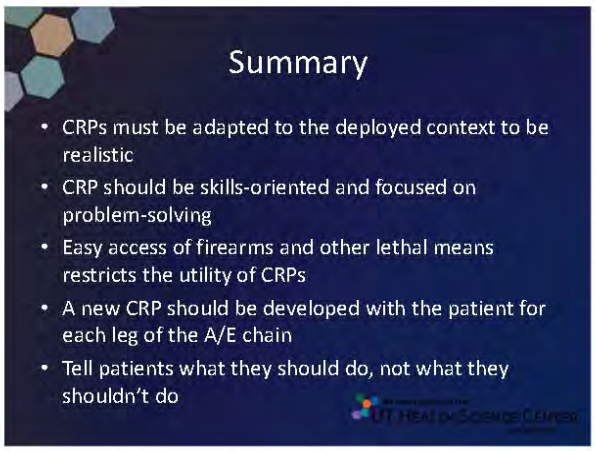

When thinking about killing myself or acting on my suicidal thoughts by trying to find a gun (or another method to kill myself), I agree to take the following steps:
1. I will try to identify specifically what's upsetting me.
2. Write out and review more reasonable responses to my suicidal thoughts, including thoughts about myself, others, and the future.
3. Review all the conclusions I've come to about these thoughts in the past in my treatment log.
4. Try and do the things that help me feel better for at least 30 mins.
5. Repeat all of the above at least one more time.
6. If the thoughts continue, get specific, and I find myself preparing to do something, I'll call the emergency call person at (phone number: XXXXXXX).
7. If I still feel suicidal and don't feel like I can control my behavior, I'll go to the emergency room located at XXXXXXX, phone number; XXXXXXX.


During the A/E process, I agree to the following behaviors:
1. Not possess weapons of any kind
2. Listen to medical staff and flight crew at all times
3. Not engage in potentially dangerous actions at any time
4. Not threaten or otherwise endanger the safety of myself, other patients, or other medical staff
5. Not to injure myself or engage in suicidal behaviors
If at any time I feel the desire to harm myself or others, I agree to tell medical staff immediately


Secrets to successful crisis planning
• View plan as a clinical intervention, not a risk management strategy
• Work with the patient to develop the plan
• Sit next to the patient when creating the plan
• Skills training!!!
• Practice, practice, practice
• In combat zones, CRP should be appropriate to context/situation, and should be revisited at each leg in A/E chain


I will use this crisis response plan when:
1. Wanting to go to sleep and not wake up
2. Thinking about holding a gun to my head
3. Thinking "I can't take it anymore."
Things I will do on my own for 30 mins:
1. Take slow, deep breaths
2. Think about my upcoming promotion
3. Write a letter home to my wife
If that does not work, I will contact other people:
1. Talk to Dave about hobbies
2. Talk to Beth about funny memories
If I am still in crisis, I will contact a medical professional:
1. Dr. Wood at CSC: xxx-xxxx
2. Go to CSH emergency department


I will use this crisis response plan when:
1. Feeling my heart racing
2. Feeling agitated, like I can't sit still
Things I will do on my own for 30 mins:
1. Close my eyes and take 20 deep breaths
2. Use the conveyer belt activity
3. Look through pictures of my family
If that does not work, I will contact other people:
1. Talk with escort about postdeployment plans
2. Ask escort to play cards
If I am still in crisis, I will contact a medical professional:
1. Tell flight doc how I am feeling


Summary
• CRPs must be adapted to the deployed context to be realistic
• CRP should be skills-oriented and focused on problem-solving
• Easy access of firearms and other lethal means restricts the utility of CRPs
• A new CRP should be developed with the patient for each leg of the A/E chain
• Tell patients what they should do, not what they shouldn't do


Questions?
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Department of Psychiatry
University of Texas Health Science Center at San Antonio
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Trends in service members seeking combat stress services in remote deployed settings

88 MDG - WPAFB

Capt Sara Wright, Ph.D.

The purpose of this presentation is to educate medical providers on trends in service members who seek combat stress services in deployed settings. A descriptive analysis was conducted of military service members who sought combat stress services in Afghanistan from 2008 to 2010 at four forward operating bases and three combat outposts. Prevalence and ratios analyses were conducted to describe demographic information, including age, race, gender, rank, marital status, number of deployments, and history of prior mental health treatment. Information was also collected about treatment including presenting problem, diagnosis, length of treatment, psychiatric medication use, and treatment dropout rates. The demographic information collected in this project was then discussed in the context of demograghic information known about SM who were deployed to Afghanistan in similar time frame (MHAT, 2009). The information gathered can be used in several ways to better educate medical and mental health providers and policymakers about current mental health trends in deployed settings. Specifically, the information can be used to determine those who may be more at risk for developing psychological problems while deployed. In addition, the information can be used by combat stress providers to more effectively target outreach efforts to those who are likely to seek combat stress services. The information can also be used to educate combat stress providers on the types of diagnoses and treatment interventions that are used in deployed setting.

Trends in Combat Stress Patients in a Remote Deployed Setting

Sara Wright, PsyD, ABPP
Capt, USAF

Anna Fedotova, MPH
Capt, USAF

"The views and opinions expressed in this presentation are those of the authors and *do not reflect* official policy or position of the United States Air Force, Department of Defense, or US Government."

Overview

- Rationale
- Method
- Findings
  - Demographics of Service Members
  - Combat Stress Treatment Trends
- Implications
- Questions

Rationale

- Very little research in this area
  - Lots research on post deployment mental health, none on deployed mental health
  - Very little data on who is seeking services, what treatment consists of, and no data from remote areas
    - » "Outpatient Mental Health Care at a Remote U.S. Air Base in Southern Iraq" by Wayne Chappelle, 2006.
    - » M-HAT OEF VI

Method

- Bagram Air Base, Afghanistan, Joint Combat Casualty Research Team (JC2RT) determined this was a Performance Improvement Project
- Records review of combat stress patients from February 2008 – February 2010
  - Informed consent for treatment signed by all patients included statement "Your non-identifiable information may be used for performance improvement project purposes"
- 301 deployed SM
- 4 FOBs & 3 COPs in Eastern Afghanistan

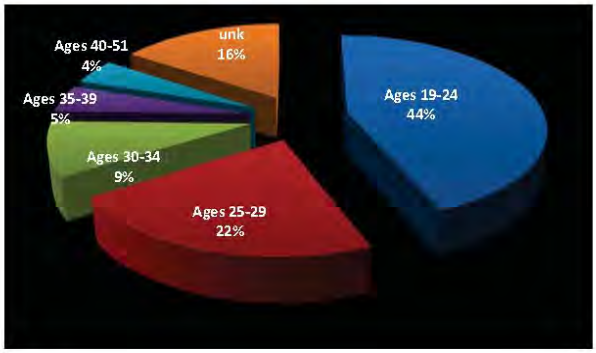
Findings

Train, Treat, Teach

- Demographics of Patients
  - Age
  - Gender
  - Ethnicity
  - Rank
  - Marital Status
  - Branch Service
  - Military Status
- Treatment
  - Referral Source
  - Diagnosis
  - Number Sessions
  - Drop Out Rates
  - Medication Usage

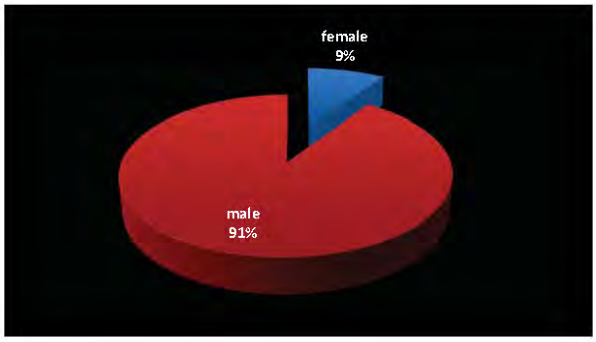
Age

Train, Treat, Teach



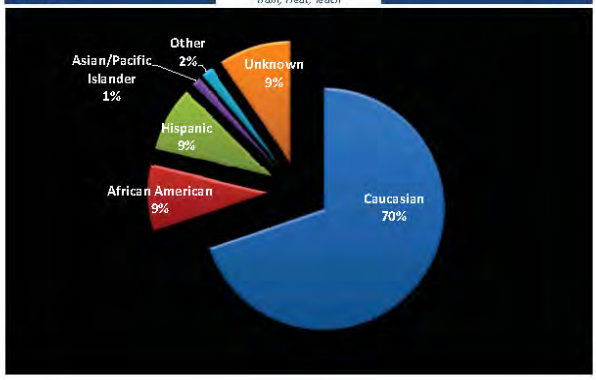
Gender

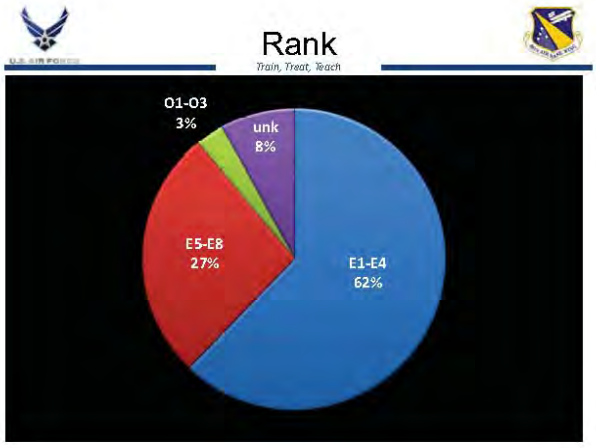
Train, Treat, Teach

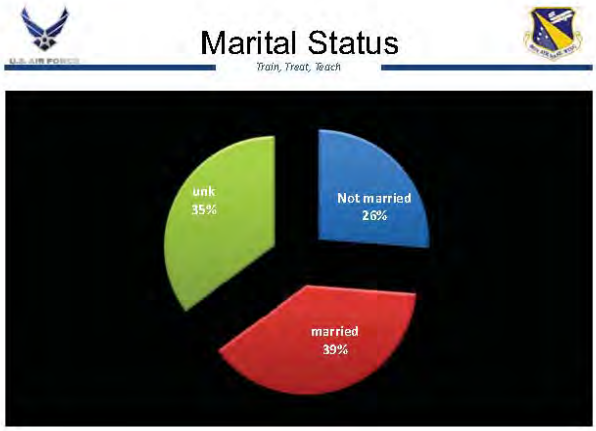


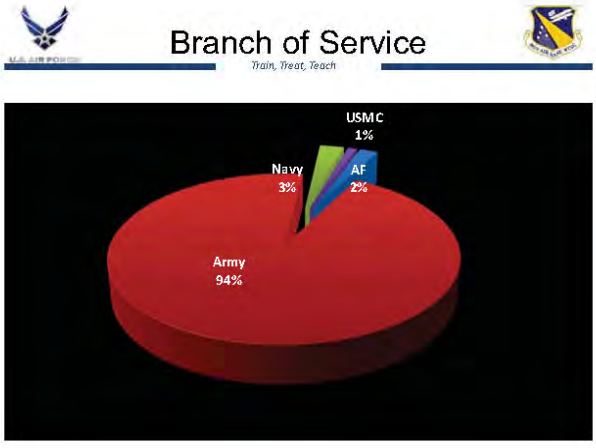
Ethnicity

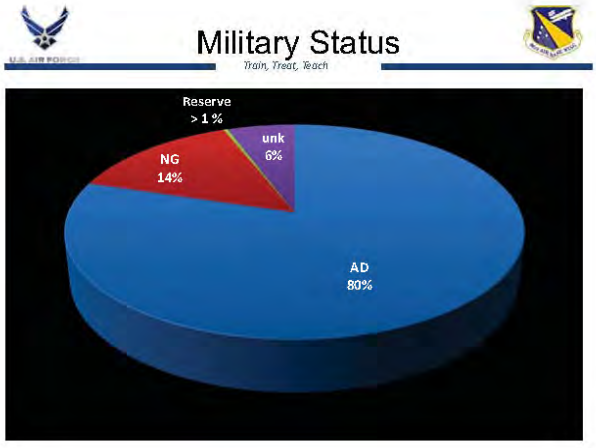
Train, Treat, Teach

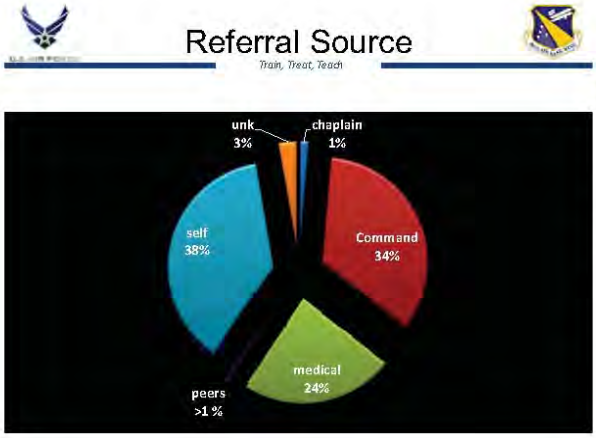


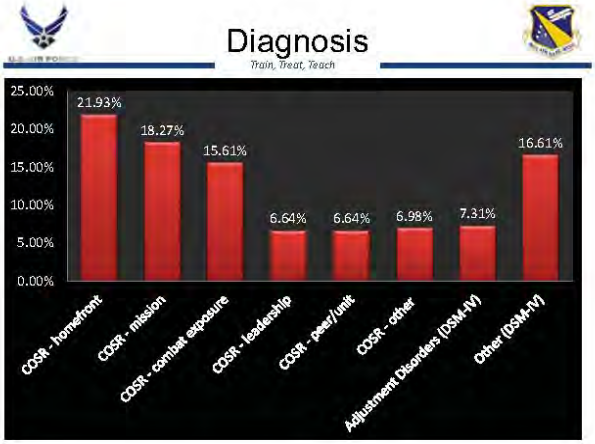

Rank
Train, Treat, Teach
O1-O3
3%
unk
8%
E5-E8
27%
E1-E4
62%

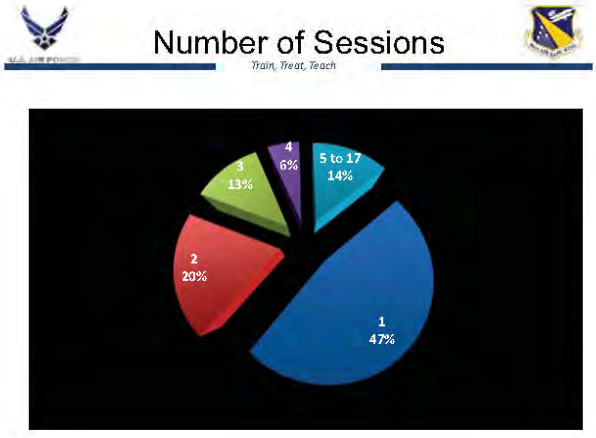

Marital Status
Train, Treat, Teach
unk
35%
Not married
26%
married
39%

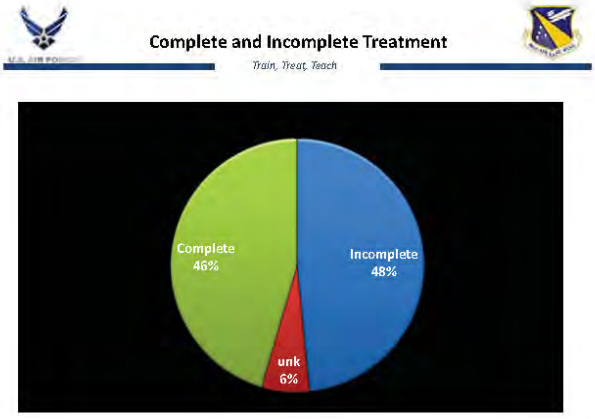

Branch of Service
Train, Treat, Teach
USMC
1%
Navy
3%
AF
2%
Army
94%


Military Status
Train, Treat, Teach
Reserve
> 1 %
unk
6%
NG
14%
AD
80%


Referral Source
Train, Treat, Teach
unk 3%
chaplain 1%
self 38%
Command 34%
medical 24%
peers >1 %

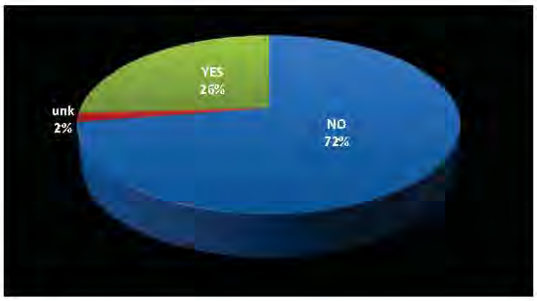

Diagnosis
Train, Treat, Teach
25.00%
20.00%
15.00%
10.00%
5.00%
0.00%
21.93%
18.27%
15.61%
6.64%
6.64%
6.98%
7.31%
16.61%
COSR - homefront
COSR - mission
COSR - combat exposure
COSR - leadership
COSR - peer/unit
COSR - other
Adjustment Disorders (DSM-IV)
Other (DSM-IV)


Number of Sessions
Train, Treat, Teach
4 6%
5 to 17 14%
3 13%
2 20%
1 47%


Complete and Incomplete Treatment
Train, Treat, Teach
Complete 46%
Incomplete 48%
unk 6%

Medication Usage

Train, Treat, Teach



Implications

Train, Treat, Teach

- Can identify those most likely to seek care
  - Help prepare mental health providers for deployment
- Importance developing relationships with referral sources
- Diagnoses most likely to encounter and treat are NOT PTSD or TBI
- Treatment is very short term and often not completed

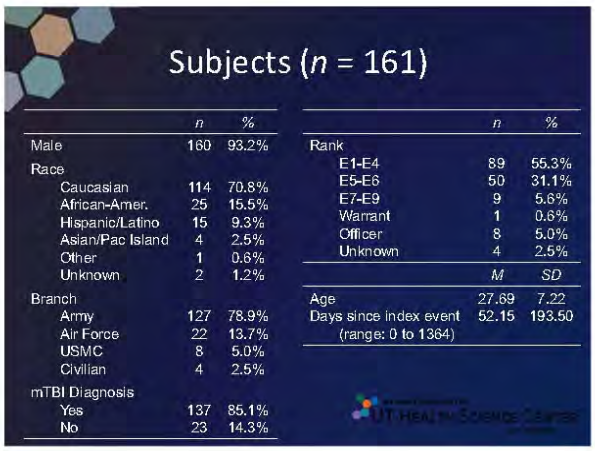
Clinical features of mTBI within days of injury in a combat zone

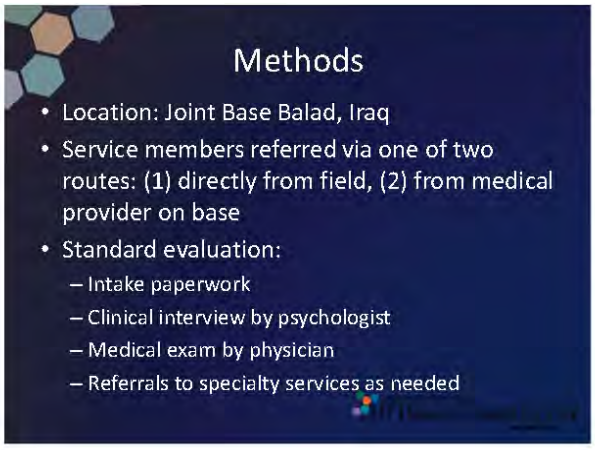
University of Texas Health Science Center at San Antonio

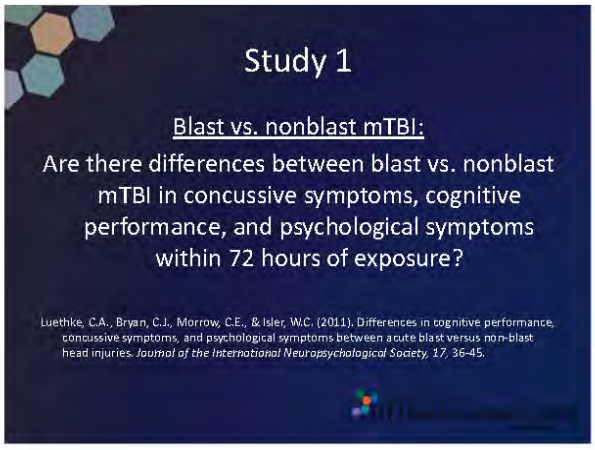
Dr. Craig Bryan

There is very limited data regarding the impact of mTBI within days of injury, which restricts deployed medical providers' ability to make optimal decisions. In the current presentation, a series of findings from a forward-deployed TBI Clinic will be reviewed: (1) absence of differences in neuropsychological functioning according to blast vs. nonblast injury mechanism; (2) clinical factors associated with clinicians' decisions to return a service member to duty; (3) variables contributing to posttraumatic headache; (4) and typical patterns of decline in neuropsychological performance on the ANAM following mTBI.


Clinical features of mTBI within days of injury in a combat zone
Craig J. Bryan, PsyD, ABPP
Assistant Professor
Department of Psychiatry
University of Texas Health Science Center at San Antonio


Subjects (n = 161)
n %
Male 160 93.2%
Race
Caucasian 114 70.8%
African-Amer. 25 15.5%
Hispanic/Latino 15 9.3%
Asian/Pac Island 4 2.5%
Other 1 0.6%
Unknown 2 1.2%
Branch
Army 127 78.9%
Air Force 22 13.7%
USMC 8 5.0%
Civilian 4 2.5%
mTBI Diagnosis
Yes 137 85.1%
No 23 14.3%
n %
Rank
E1-E4 89 55.3%
E5-E6 50 31.1%
E7-E9 9 5.6%
Warrant 1 0.6%
Officer 8 5.0%
Unknown 4 2.5%
M SD
Age 27.69 7.22
Days since index event (range: 0 to 1364) 52.15 193.50


Methods
• Location: Joint Base Balad, Iraq
• Service members referred via one of two routes: (1) directly from field, (2) from medical provider on base
• Standard evaluation:
– Intake paperwork
– Clinical interview by psychologist
– Medical exam by physician
– Referrals to specialty services as needed


Study 1
Blast vs. nonblast mTBI:
Are there differences between blast vs. nonblast mTBI in concussive symptoms, cognitive performance, and psychological symptoms within 72 hours of exposure?
Luethke, C.A., Bryan, C.J., Morrow, C.E., & Isler, W.C. (2011). Differences in cognitive performance, concussive symptoms, and psychological symptoms between acute blast versus non-blast head injuries. Journal of the International Neuropsychological Society, 17, 36-45.

Clinical features

	Nonblast		Blast		χ^2	p
	n	%	n	%		
Disposition RTD	40	95.2	37	92.5	0.268	0.604
LOC Duration					**8.603**	**0.035**
None	19	45.2	25	62.5		
< 1 min	9	21.4	12	30.0		
1 - 20 mins	12	28.6	3	7.5		
20+ mins	2	4.8	0	0		
Dazed & confused	37	88.1	33	84.6	0.209	0.648
Amnesia for index event	21	51.2	15	38.5	1.314	0.252
Bruising / laceration / swelling	**33**	**78.6**	**11**	**29.7**	**19.017**	**0.000**

Immediate concussive symptoms

	Nonblast		Blast		χ^2	p
	n	%	n	%		
Dizziness	28	66.7	22	55.0	1.172	0.279
Memory	19	45.2	11	27.5	2.779	0.096
Balance	**19**	**45.2**	**10**	**25.0**	**3.671**	**0.055**
Nausea	**22**	**52.4**	**8**	**20.0**	**9.259**	**0.002**
Vomiting	**11**	**26.2**	**3**	**7.5**	**5.055**	**0.025**
Concentration	19	45.2	12	30.0	2.023	0.155
Irritability	8	19.0	8	20.0	0.012	0.913
Vision	12	28.6	7	17.5	1.411	0.235
Hearing	**7**	**16.7**	**21**	**52.5**	**11.699**	**0.001**
Sleep	14	33.3	15	37.5	0.156	0.693

Current concussive symptoms

	Nonblast		Blast		χ^2	p
	n	%	n	%		
Memory	13	31.0	8	20.0	1.290	0.256
Balance	5	11.9	3	7.5	0.451	0.502
Nausea	3	7.1	2	5.0	0.164	0.685
Vomiting	1	2.4	1	2.5	0.001	0.972
Concentration	15	35.7	8	20.0	2.507	0.113
Irritability	6	14.3	9	22.5	0.925	0.336
Vision	4	9.5	5	12.5	0.186	0.666
Hearing	4	9.5	9	22.5	2.586	0.108
Sleep	9	21.4	7	17.5	0.201	0.654

Current psych symptoms

	Nonblast		Blast		t	p
	M	SD	M	SD		
PCL-M	26.65	13.22	27.77	8.91	-0.980	0.330
Global Mental Health	3.39	0.58	3.48	0.38	0.167	0.868
Insomnia Severity Index	8.20	6.60	7.71	5.97	0.166	0.869
ANAM Mood Scales						
Sleep	2.95	1.36	2.91	1.27	0.184	0.854
Happiness *	54.73	24.70	61.97	22.60	-1.409	0.163
Vigor *	45.03	22.64	53.34	22.28	-1.803	0.075
Fatigue *	37.28	24.26	32.17	24.33	1.144	0.256
Restlessness *	20.20	18.76	22.60	20.38	-0.564	0.574
Anxiety *	16.68	17.70	15.69	16.69	0.131	0.896
Depression *	16.83	20.86	9.34	17.28	1.681	0.097
Anger *	18.03	20.86	21.29	20.71	-0.773	0.442

* Percentile scores

ANAM score declines: Baseline to postinjury

Subtest		Speed				Accuracy			
		Nonblast		Blast		Nonblast		Blast	
		M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
SRT	Baseline	100.88	16.26	101.78	7.81	101.22	0.85	101.31	1.01
	Postinjury	74.42	38.06	75.44	51.65	101.04	0.21	101.12	0.33
	ΔM	26.46	43.18	26.33	50.25	0.17	0.83	0.19	0.98
PRT	Baseline	99.50	17.47	96.74	15.01	99.83	11.96	101.92	8.74
	Postinjury	68.88	78.33	72.89	52.09	102.57	10.49	88.73	35.29
	ΔM	30.62	79.75	23.85	51.29	2.52	15.55	13.19	34.48
LRN	Baseline	98.42	14.46	96.56	13.69	104.13	9.96	105.62	6.26
	Postinjury	88.65	27.20	91.04	21.76	104.00	9.77	105.77	8.25
	ΔM	9.77	24.82	5.12	22.17	0.13	7.36	0.15	7.58
DM	Baseline	92.38	16.85	88.52	21.91	105.70	10.84	104.19	9.44
	Postinjury	79.65	27.51	70.78	39.56	96.17	18.52	98.96	17.11
	ΔM	12.73	24.70	17.74	30.85	5.92	20.30	3.56	19.01
WM	Baseline	85.77	27.99	80.59	27.28	108.00	6.85	112.04	4.12
	Postinjury	73.15	30.43	75.89	30.17	104.78	9.10	108.58	9.18
	ΔM	12.62	22.05	4.70	17.52	2.69	9.41	4.67	10.92
SM	Baseline	94.15	16.67	96.89	18.57	106.96	6.43	105.65	5.53
	Postinjury	79.38	30.15	86.56	24.37	95.35	19.07	104.23	8.34
	ΔM	14.77	26.74	10.33	19.53	12.46	20.45	1.37	10.63

Conclusions

Blast injuries associated with less severe LOC and concussive symptoms immediately following index event (except hearing problems)

Blast injuries and nonblast injuries do not differ in terms of concussive symptoms, psychological symptoms, or neuropsychological impairment within 72 hours of index event

Study 2

TBI vs. no TBI:

What proportion of service members demonstrate declines in ANAM scores relative to baseline performance during an mTBI evaluation conducted in Iraq?

Bryan, C.J., & Hernandez, A.M. (under review). Magnitudes of Decline on ANAM Subtest Scores Relative to Predeployment Baseline Performance Among Service Members Evaluated for Traumatic Brain Injury in Iraq.

	TBI								No TBI				No TBI vs. TBI with No LOC		
	LOC Duration														
	No LOC (n = 32)		< 1 min (n = 11)		1-20 mins (n = 9)		20+ mins (n = 2)		No LOC (n = 19)						
	n	%	n	%	n	%	n	%	n	%			χ^2	*P*	*Φ*
Speed															
SRT	15	46.9%	4	36.4%	6	66.7%	1	50.0%	1	5.3%			9.588	.002	0.434
PRT	21	65.6%	4	36.4%	5	55.6%	1	50.0%	4	21.1%			7.779	.005	0.403
CSL	16	50.0%	3	27.3%	5	55.6%	0	0.0%	2	10.5%			6.984	.008	0.378
CSD	17	53.1%	3	27.3%	4	44.4%	1	50.0%	4	21.1%			5.063	.024	0.315
MATH	16	50.0%	3	27.3%	7	77.8%	1	50.0%	4	21.1%			4.191	.041	0.287
SM	15	46.9%	3	27.3%	6	66.7%	1	50.0%	4	21.1%			3.401	.065	0.258
Accuracy															
SRT	1	3.1%	0	0.0%	0	0.0%	0	0.0%	0	0.0%			0.606	.436	0.109
PRT	10	31.3%	2	18.2%	5	55.6%	1	50.0%	4	21.1%			0.622	.430	0.110
CSL	3	9.4%	2	18.2%	1	11.1%	0	0.0%	1	5.3%			0.279	.597	0.074
CSD	5	15.6%	4	36.4%	4	44.4%	1	50.0%	3	15.8%			0.000	.988	0.002
MATH	8	25.0%	1	9.1%	5	55.6%	0	0.0%	4	21.1%			0.103	.748	0.045
SM	10	31.3%	2	18.2%	4	44.4%	1	50.0%	2	10.5%			2.846	.092	0.236

Conclusions

- ANAM speed scores sensitive to mTBI
  - 50% or more of service members with mTBI (regardless of LOC severity) show > .5 SD (7.5 points) decline in ANAM speed standard score
  - Only 10-25% of service members without mTBI show same magnitude of declines
- ANAM accuracy scores do not differentiate by mTBI status
  - Simple reaction time seems especially robust

Study 3

Headache predictors:

Which concussive, psychological, and cognitive symptoms are associated with headache severity among deployed military personnel deployed with mTBI?

Bryan, C.J., & Hernandez, A.M.*(2011). Predictors of posttraumatic headache severity among deployed military personnel. *Headache, 51*, 945-953.

Full sample (*n* = 137)

	b	SE	95% C.I. Lower	95% C.I. Upper	*exp(B)*	95% C.I. Lower	95% C.I. Upper	*P*
Intercept	1.082	0.155	0.777	1.386	2.949	2.175	4.000	< .001
LOC	0.210	0.099	0.017	0.404	1.234	1.017	1.498	.033
TBI symptoms	0.019	0.017	-0.015	0.053	1.019	0.985	1.055	.277
PCL	0.009	0.003	0.002	0.015	1.009	1.002	1.015	.008
Reaction Time	-0.001	0.001	-0.002	0.000	0.999	0.998	1.000	.035
Zero-inflation								
Intercept	-0.506	0.383	-1.256	0.244	0.603	0.285	1.276	.186
ISI	-0.096	0.037	-0.169	-0.022	0.909	0.845	0.978	.011

Patients seen w/i 7 days (*n* = 101)

	b	SE	95% C.I. Lower	95% C.I. Upper	*exp(B)*	95% C.I. Lower	95% C.I. Upper	*P*
LOC	0.317	0.127	0.068	0.566	1.373	1.071	1.761	.013
TBI symptoms	0.026	0.024	-0.021	0.073	1.026	0.980	1.075	.276
PCL	0.013	0.005	0.003	0.022	1.013	1.003	1.022	.007
Reaction Time	-0.003	0.001	-0.006	0.000	0.997	0.994	1.000	.024
Zero-inflation								
Intercept	-0.487	0.468	-1.404	0.430	0.615	0.246	1.537	.298
TBI symptoms	-0.169	0.100	-0.365	0.027	0.844	0.694	1.027	.090

Conclusions

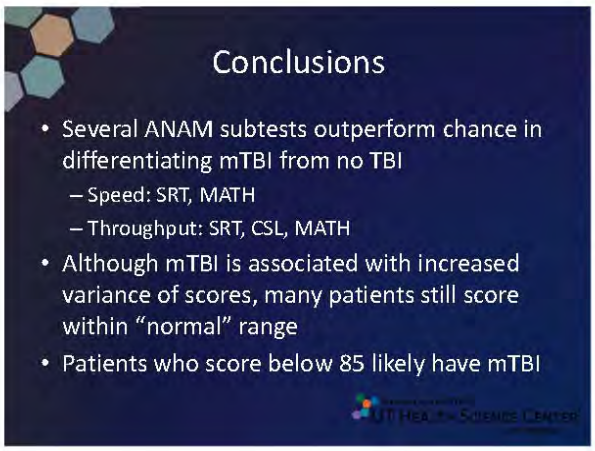
- Headache severity following mTBI is associated with LOC, PTSD symptoms, slowed reaction time, and insomnia severity
- Within 7 days of index mTBI, TBI symptoms appear to be more robust than insomnia

ANAM sensitivity

Can the ANAM subtest scores differentiate between deployed service members with and without mTBI within 72 hours of index event?

ANAM Subtest	AUC	SE	p	95% C.I. Lower	95% C.I. Upper
Speed					
SRT	.682	.073	.023	.540	.825
PRT	.585	.076	.290	.436	.734
CSL	.636	.076	.091	.487	.785
CSD	.605	.079	.193	.449	.760
MATH	.672	.073	.032	.529	.815
SM	.571	.080	.379	.414	.728
Accuracy					
SRT	.552	.081	.515	.393	.712
PRT	.606	.077	.187	.456	.757
CSL	.499	.080	.986	.343	.654
CSD	.614	.080	.158	.457	.770
MATH	.482	.076	.819	.332	.631
SM	.507	.082	.933	.346	.668
Throughput					
SRT	.681	.073	.024	.538	.824
PRT	.592	.075	.253	.444	.739
CSL	.682	.072	.024	.541	.823
CSD	.624	.077	.121	.474	.775
MATH	.680	.073	.025	.537	.822
SM	.542	.081	.600	.382	.702

ANAM Subtest	Standard Score	Sensitivity	Specificity	Accuracy	PPV	NPV
SRT Speed	70	0.143	1.000	0.572	1.000	0.380
	85	0.200	0.952	0.576	0.888	0.396
	100	0.514	0.667	0.591	0.746	0.519
	115	0.971	0.000	0.486	0.649	--
MATH Speed	70	0.200	0.905	0.553	0.800	0.396
	85	0.457	0.762	0.610	0.785	0.492
	100	0.829	0.381	0.605	0.718	0.754
	115	0.971	0.143	0.557	0.683	0.948
SRT Throughput	70	0.143	1.000	0.572	1.000	0.380
	85	0.257	0.905	0.581	0.837	0.414
	100	0.714	0.619	0.667	0.781	0.647
	115	0.943	0.048	0.496	0.654	0.902
CSL Throughput	70	0.086	1.000	0.543	1.000	0.365
	85	0.257	0.905	0.581	0.837	0.414
	100	0.571	0.619	0.595	0.741	0.550
	115	0.886	0.143	0.515	0.663	0.822
MATH Throughput	70	0.057	1.000	0.529	1.000	0.358
	85	0.171	0.905	0.538	0.774	0.388
	100	0.657	0.667	0.662	0.790	0.605
	115	0.971	0.095	0.533	0.671	0.948


Conclusions
• Several ANAM subtests outperform chance in differentiating mTBI from no TBI
– Speed: SRT, MATH
– Throughput: SRT, CSL, MATH
• Although mTBI is associated with increased variance of scores, many patients still score within "normal" range
• Patients who score below 85 likely have mTBI


Questions?
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